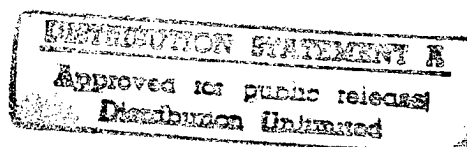


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1ST INTERNATIONAL CONFERENCE
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1st INTERNATIONAL CONFERENCE
ON INTELLIGENT MATERIALS

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INTRODUCTION TO THE SUBJECT

Intelligent materials have the ability to respond to environmental conditions intelligently, and manifest intelligent functions such as, sensing, processing and actuating.

These materials are expected to act as a catalyst for innovation in many technological fields for example information science, electronics, life and medical science and safety engineering.

The credibility, future potential and world-wide interest in this area were well appreciated by the success of "The International Workshop on Intelligent Materials" held from March 15 to 17, 1989 in Tsukuba Science City, Japan, and also by the release of new publication of "Journal of Intelligent Materials Systems and Structures" in USA.

In order to promote this emerging technology of an interdisciplinary nature, and also to maintain constant contact among various type of specialists and practitioners concerned, the Intelligent Materials Forum (IMF) was established with the support of Science and Technology Agency of Japan.

This conference is organized by the IMF for the purpose of opening an international channel for furnishing information on technologies applicable and discussing common research interests by many scientists and researchers of the subject.

Preface

The research and development of intelligent materials are a new and rapidly evolving field which is bringing researchers together from many diversified fields, such as medicine, biomaterials, aeronautics, materials science and computer engineering.

The newly created concepts of "intelligent materials" are based on advanced developments in both materials and information sciences. The general goals are set towards the creation of intelligent materials and tailor these artificially formed materials to function with the provide combinations of sensor, information processor, effector, and feedback/feedforward characteristics within the materials themselves.

In Japan, these concepts were debated from July, 1987 through November, 1989 under the sponsorship of the Council for Aeronautics, Electronics and Other Advanced Technologies, the Science and Technology Agency of the Japanese government.

This program brought together specialists from diversified fields, viz. science, chemistry, electronics and information science, life and medical science, and safety engineering. Subsequently, International Workshop on Intelligent Materials was held in Tsukuba, Japan in March, 1989.

Further, in continuation to this workshop, a joint US-Japan Workshop on Smart/Intelligent Materials and Systems was held in Honolulu, Hawaii in March, 1990. Also, publication of the Journal of Intelligent Materials Systems and Structures and the Journal of Intelligent Materials (in Japanese) were brought out in 1990 in the U.S. and in 1991 in Japan, respectively.

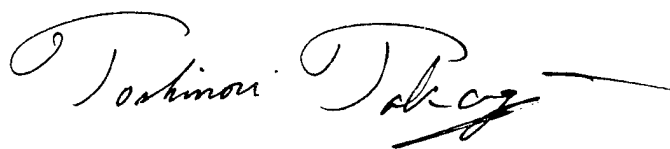
And now, the First International Conference on Intelligent Materials is held in Oiso, Japan, under the organization of Intelligent Material Forum setup within the Society of Non-Traditional Technology and supported by Science and Technology Agency of the Japanese government.

The goal of this Conference is to expand the flow of new ideas and information across the different boundaries of research. By bringing together the specialists from the various research and application fields, this Conference is hoped to enhance the communication between them in their interdisciplinary field studies and help search for means to think about intelligent materials.

More than 100 papers have been submitted at this Conference from the various countries, despite the first conference. The credits for the success of this Conference goes to the excellent cooperation of authors and the members of the Conference committee.

On behalf of organization, I would like to thank all those involved for their help in making this Conference a great success.

Finally, as general chairman of the Conference committee, I wish all the participants a fruitful experience at the Conference.

A handwritten signature in cursive script, reading "Toshinori Takagi", followed by a horizontal line.

Toshinori Takagi

General chairman

Professor-Emeritus of Kyoto University

A Perspective of the Intelligent Materials

Toshinori Takagi

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The concept of intelligent material is a newly developed concept and the intelligent materials is a complex material science subject in which the material is treated to possess functional properties with the capabilities to act a sensor, processor, an effector and further, have the feedback/feedforward abilities in the material itself.

The purpose of establishing this new scientific field is to achieve more functional and complete systematic qualities such as recognition, discrimination, adjustability etc., with the use of intelligent materials. The intelligent material is a subject with a wide area of interest to researchers in the interdisciplinary fields such as medicine, pharmacy, biomaterial, engineering and electronics engineering.

Conceptionally, it may be predicted that in the future the hardware and software combined together to achieve a firmware which intone will be an intelligent material. For example, this may correspond to many forms of life which is controlled autonomously according to the environmental changes.

Intelligent materials can be defined as materials which react to environmental changes at the more optimum conditions and manifest their own functions as per the requirements necessitated by the changes.

In japan, from july 1987 to november 1989 the subject was discussed within the official organ of council for Aeronautics, Electronics and Other Advanced Technologies of Science and Technology Agency. The discussion was the first one to call for defining the concept clearly by the specialists in the various different research and application fields as mentioned above.

In this paper, the recent situation about the intelligent materials and their research activities in japan are discussed and reported.

Intelligent Foreseeing of Fracture in CFGFRP Composites by the Measurement of Electrical Resistance

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For the foreseeing of fracture, it is necessary to know the strain in the material induced by stress. The authors found out a change in electrical resistance on straining, and a change in residual resistance after straining for carbon fiber bundles in CFGFRP(carbon fiber-glass fiber reinforced plastics) composites. This means that CFGFRP composites have the ability to memorize the maximum strain applied to the material as a residual change in the electrical resistance. This ability is useful in estimating intelligently the maximum strain applied to CFGFRP composites in the past and as both a safety check for structural materials and as a sensor to judge when to repair or exchange the material. The present research was originally undertaken to establish a new method of foreseeing the fracture of CFGFRP composites through the measurement of the residual resistance of carbon fiber bundles after straining.

Three kinds of carbon fiber(PAN-HSCF; PAN-based high strength, PAN-HMCF; PAN-based high modulus and Pitch-HPCF; Pitch-based high property carbon fiber) were evaluated for their suitability for foreseeing the fracture of CFGFRP composites. Resistance of these carbon fiber bundles were $244\mu\Omega\text{cm}$, $263\mu\Omega\text{cm}$ and $148\mu\Omega\text{cm}$ respectively for PAN-HSCF, PAN-HMCF and Pitch-HPCF. Tensile strength and elongation of these fibers and of glass fibers were 400 kg/mm^2 , 300 kg/mm^2 , 260 kg/mm^2 and 150 kg/mm^2 ; and 1.7%, 0.9%, 0.8% and 4.8%, respectively. Samples containing 4.3V% PAN-HSCF, 3.9V% PAN-HMCF, 9.0V% Pitch-HPCF along with 31.6V% glass fiber in each sample in a vinylester matrix with a cross sectional area of 64 mm^2 were strained at a rate of 1 mm/min in tension with a gage length of 450 mm. The electrical resistance of the carbon fiber bundles was determined by a two-terminal dc method($I = 1\mu\text{A const.}$) during and after straining. The load of CFGFRP composites increased linearly with the strain, but changes in electrical resistance showed unique curves as a function of strain. A residual, permanent increase in the electrical resistance was observed, and the relative ratio of residual resistance increased nonlinearly with strain. Therefore, it is possible to foresee fracture by measurement of the residual resistance of CFGFRP composites even after straining. Further, it was also found that residual resistance of CFGFRP composites containing PAN-HSCF was larger than that for samples containing PAN-HMCF and Pitch-HPCF. PAN-HSCF were more suitable for use in this application than PAN-HMCF and Pitch-HPCF. The observed resistance change of the carbon fiber bundles in these composites is assumed to relate to the degree of fracture and misorientation of the carbon fiber bundles during straining. This new method of the measuring the residual change in electrical resistance of carbon fiber bundles was found to be a promising method for foreseeing the fracture in CFGFRP composites.

Characteristics of GaAs Molecular Layer Etching

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Processing techniques with atomic scale controllability will be important to fabricate super ultra large scale integration devices and quantum devices in the next generation. For this etching process, we study layer-by-layer etching of GaAs. In this paper, we report the molecular layer etching (MLE) process that consists of sequentially controlled feeding of Cl etchant and applying of low energy Ar ion beam to the substrate.

In the experiment, we use an ECR (Electron Cyclotron Resonance) plasma etching system which is evacuated to the background pressure of about 7×10^{-7} Pa. An XPS (X-ray Photoelectron Spectroscopy) system is provided for surface analysis. A sample is transferred between the ECR chamber and the XPS chamber without exposure to air.

During etching process, the Ar ECR discharge is maintained in the etching chamber and working pressure is about 6×10^{-2} Pa. At the first part, the etchant of Cl₂ gas, which flow rate is 0.0035 sccm, is fed into the ECR chamber and Cl radical excited by Ar plasma is adsorbed to the sample surface. At the second, remaining Cl₂ gas is purged out from the ECR chamber. At the third, low energy Ar ion beam accelerated by bias voltage 20V is irradiated on the sample. Finally etching products are purged out. One etching cycle consists of these four parts.

The amount of Cl radical adsorption on the GaAs surface, which is determined by XPS as the function of Cl₂ gas feeding time, saturates at the feeding time between 7s and 15s for one monolayer, and between 32s and 40s for trimonolayer.

Under the monolayer adsorption condition of Cl radical, which parameters are Cl₂ feeding time of 10s, Cl₂ purging time of 100s and etching product purging time of 1s, it is found that the etching rate (Å/cycle) is independent of Cl feeding time and Ar beam irradiation time and saturates at one GaAs molecular layer etching cycle.

Under the molecular layer etching condition, the etching damage is estimated by the DLTS method. After etching sequence of 60 cycles, induced damage by the etching is investigated. In comparison with Ar IBE (50eV 6min), it is very low.

In conclusion it is emphasized that the MLE (Molecular Layer Etching) technique is achieved. It is independent of the etchant feeding time and Ar ion beam irradiation time, and is very low damage.

Control of Molecular Orientation in Organic Thin Films with The Ionized-Cluster-Beam Technique

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Superstructure control is very important to the realization of organic materials with excellent functions. Molecular orientation has a large influence on material properties, especially in systems made up of anisotropic molecules. Thin films of nonlinear optical (NLO) materials are typical examples. Third order NLO materials play an important role in optical switching devices and memory devices. Among the wide variety of materials being studied for use in such devices, organic materials with a π -conjugated system have noteworthy characteristics that enable an ultrafast response. It is possible to construct an ultrafast optical system using semiconductor laser diodes if films can be obtained with a larger $\chi^{(3)}$ value than those currently available. Two possible approaches to obtaining a large $\chi^{(3)}$ value are as follows; i) molecular design and ii) the alignment of molecular polarization with the electric field of the incident light through molecular orientation control. In this study, we focused on the second approach and examined the feasibility of the ionized-cluster-beam (ICB) technique.

We used terephthal-bis[(p-N,N-diethylamino)aniline] (SBA) as a deposition material. The material has a large $\chi^{(3)}$ value compared to typical NLO polymers despite its short π -conjugation system. It was loaded in a graphite crucible and evaporated. Microcrystalline films were grown on Corning 7059 glass, the cleaved surface of MoS₂ and rubbed poly(p-phenylene vinylene) (PPV) film. The morphology of the films was observed with a SEM.

When Corning glass was used as a substrate, microcrystals 1 μ m wide grew at a low acceleration voltage (Ea). The substrate surface was not completely covered with microcrystals, and the microcrystals had no specific orientation. Molecular migration on the substrate must be enhanced to improve the orientation.

On the cleaved surface of MoS₂, the microcrystals were aligned in three directions which intersected each other at angles of 120°. This orientation is due to the atomic arrangement of the substrate material. The largest microcrystals were 1 μ m wide and 5 μ m long. It was difficult to improve the orientation by varying the Ea. An attempt was made to achieve a preferred orientation through migration enhancement by setting the substrate obliquely during deposition. However, this was unsuccessful.

A PPV film uniaxially oriented by rubbing was used as a substrate in an oblique arrangement. The molecular structure of PPV is very similar to that of SBA. Microcrystals several μ m long were observed to form. Although the orientation of the microcrystals was ambiguous in film prepared without ionization, it was improved by ionization and acceleration. At a high Ea, we successfully obtained microcrystals of about 5 μ m in length which were preferably oriented perpendicular to the rubbing direction. Spectroscopic investigation revealed that the SBA molecules in the microcrystals aligned themselves in the rubbing direction. Therefore, all the molecules on the substrate align themselves in the same direction. The direction of the long axis of the SBA molecules is the same as that of the substrate monomer unit. This indicates that there is an interaction similar to the epitaxial effect reported for rubbed polydiacetylene.

In summary, we have confirmed that unidirectional orientation of long and planar SBA molecules is possible with the ICB technique combined with an appropriate substrate. It is important i) to use substrates which have one orientation direction, ii) to use substrates which have a structure similar to that of the materials to be deposited.

Study on the Triggering Factor of Neurite Outgrowth Using PC12 Cell

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How to control the neurite outgrowth is the basis for the formation of artificial nerve cell networks. Among various factors which may control the neurite outgrowth, nerve growth factor (NGF) is one of most well characterized ones. NGF promotes the neurite outgrowth of PC12 cells. Such an effect of NGF, however, does not obey the all-or-none principle on the triggering of the neurite outgrowth. Recently, the authors have found that ambiguous effect of NGF seems due to the influence of coexisting cells. This paper describes the effect of the cell density on the NGF action to PC12h-AG8 cells.

Methods

Cells were placed in the culture dishes at various cell density and the ratio of the neurite bearing cells to the total cells was measured. As the extreme condition, we introduced the lone cell culture system; only one cell in each well. Using this system, we examined the effect of NGF and the supernatant of the used medium on the neurite outgrowth initiation. The supernatant was mixed with the fresh medium by the ratio 1:1. The antibody to NGF receptor was incorporated to speculate the involvement of the NGF receptor.

Results

When NGF was added to the culture medium, the neurite outgrowth was promoted remarkably. The extent of outgrowth depended on the cell density in the range of 10^2 - 10^4 cells·ml⁻¹. On the other hand, the neurite outgrowth was observed also without addition of NGF. In this case, the extent of the outgrowth also depended on the same cell density range as above; i.e. as the cell density increases the outgrowth rate increases. These results suggest that coexisting cells may influence the neurite outgrowth process. In order to eliminate the effect of coexisting cells, we have a novel system of lone cell culture. Under this condition, when NGF was added to the medium, lone cells projected neurite (58%). But without NGF, none of lone cell projected neurite at all. Then we cultured lone cell using a mixture of fresh and used media. As the results, lone cell projected neurite without NGF (18%). When antibody to NGF receptor was added to the medium, number of lone cell which projected neurite decreased remarkably (2%). Therefore some factors active for the neurite outgrowth exist in the used medium, which might have been secreted from coexisting cells, and they can act on the nerve cell mostly via the NGF receptor. These factors, however, were not so effective for the maintenance of the neurite. In order to maintain and support the neurite for long time, the existence of other cells was necessary.

Three-dimensional Laser Manipulation of Microspheres and Its Role in Micromachining

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Laser trapping/manipulation of individual microspheres is essentially based on a light momentum change accompanied by refraction of a laser beam with a microsphere.¹⁾ Indeed, various microspheres such as polymer latices, oil droplets, biocells, and so forth can be freely manipulated in three-dimensional space by a laser trapping technique.²⁾ Quite recently, we developed a multi-beam laser scanning micromanipulation system, by which an arbitrary number of a microsphere can be manipulated independently by laser beams.^{3,4)} As a possible application of the technique to micromachining, we explored photochemical assembling and fixation of polymeric microspheres in solution.⁴⁾

Two polystyrene (PSt) latex particles were independently manipulated in ethylene glycol solution containing polymerizable vinyl monomers by two trapping laser beams (1064 nm). A picosecond 355 nm laser pulse was further irradiated to the contacting area of the two particles to induce photopolymerization in solution. After pulse laser irradiation for several seconds, two PSt particles were confirmed to be tightly fixed with each other. Assembling of any desired number of PSt can be done by repeating the manipulation/photopolymerization procedures. Furthermore, active movement of an integrated structure composed of three PSt particles was also shown to be possible by laser scanning micromanipulation.

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Automatically Position Controlled System with High Tc Oxide Superconductor

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Recently, Murakami et al. has developed new process¹⁾ for $\text{YBa}_2\text{Cu}_3\text{O}_{7-x}$ (YBCO) oxide superconductor; MQMP(melt quench melt powdering growth) method which promised high J_c and high levitation force. The YBCO ceramics sintered by MQMP method has strong pinning force for trapped flux, because of existence of Y_2BaCuO_5 pinning center.

After YBCO ceramics was cooled down at 77 K by liquid nitrogen, a permanent magnet was released above it. The magnet could be supported by levitation force completely above the YBCO. A levitation force and a lateral force worked on permanent magnet was measured as a function of movement distance. The measuring system used here was described elsewhere²⁾ in detail. Firstly, the magnet was lowered to the surface of the superconducting YBCO, then raised for vertical direction. As decreasing the distance between the magnet and YBCO, repulsive force was observed. Inversely, increasing the distance, attractive force was observed. When the permanent magnet was moved cyclically for the vertical direction, a large hysteresis curve on interactive force was observed. This means that there is a certain position at which attractive force was equilibrium with repulsive force. At this position attractive force and repulsive force was equilibrium. When an external force works the magnet moving it away or bringing it close to the surface of the YBCO, magnetic interaction force appears to offset the external force. So that the permanent magnet can settle automatically(without any external control) at the stable position.

The area of hysteresis loop was proportional to the time constant of dynamic stiffness. The same relationship was observed for lateral direction.

The combination of superconducting YBCO ceramics and a permanent magnet can be applied for a magnetic bearing or a magnetic suspension system without any external control system.

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An STM study of microscopic function at the interface of organic films

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Functions attributed to an atomic scale structure is considered to be one of the essential factors of intelligent materials. The possibility of microscopic function is expected to be found in the interface regions between different materials. In this experimental study, typical interfaces between inorganic materials and organic materials, and an interface between amorphous chalcogenide $a\text{-As}_2\text{Se}_3$ and HOPG were investigated by an STM and an STS in order to find a property and function which can be used in an intelligent material. Cleaved surfaces of HOPG and (100) surfaces of Si single crystals were used as inorganic substrates. The films of polysilane with a thickness of several 100 Å were formed by spin coating method, organic perylene film was evaporated by the ICB method and chalcogenide $a\text{-As}_2\text{Se}_3$ film was fabricated by evaporation. The organic films are semiconducting, and some of them are known to have photoconductivity. At the interface between polysilane and the Si single crystal, in that between perylene film and HOPG, and in that between the chalcogenide film and HOPG, strong nonlinear relations between current, I , and voltage, V , were found. At the above mentioned interfaces, the voltage regions where the I - V nonlinearity was observed are fairly wide. We are finding the modulation effect of nonlinearity by irradiation of light. By combining interface functions, the effect caused by illumination and some other junctions of the materials we expect to produce intelligent materials.

Possible nanometer scale intelligent memories

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As a future trend of microelectronic devices, nanometer scale memories are very interesting. In this experiment, nanometer scale indentation has been successfully achieved and also observed by an STM on a chalcogenide thin film of As_2Se_3 . An As_2Se_3 thin film was evaporated on an atomic order flat cleaved surface of HOPG. An evaporated As_2Se_3 film has an amorphous form at room temperature, and the thickness of the films is about 1000\AA . Since it is known that phase separation due to a spinodal decomposition mechanism in amorphous As_2Se_3 is enhanced by the application of high electric fields, we expect that some structural changes associated with the phase separation can be caused by applying a high voltage with an STM. It was found that the STM image of the surface was modified by applying about 10V for a short period. The modified part of the surface was observed as a mesa with a diameter of several tenths of nanometer with an STM as a result of the decrease in the resistivity of the As_2Se_3 films by the appearance of As clusters formed by the high-field-induced phase separation. The diameter of the mesa was apparently changed depending on the length of the period of applying high voltage. As the mesa is so clearly formed, this modification can be utilized as a new media of the nanoscale memory in principle.

We are endeavoring to fabricate chalcogenide thin films on several substrates with laminated layers in order to endow intelligent function and to improve the S/N ratio in operation for the memory.

PREPARATION OF HIGHLY ORIENTED POLY-DIACETYLENE LB-FILMS WITH ION BEAM IRRADIATION

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Thin Layer films of poly-diacetylene compounds have a great potential for the application in optoelectronics because a very large third-order non-linear susceptibility with a very fast response is obtainable with these films. However, this optical susceptibility is based on the polarization of molecules; the π -conjugation length and the polarization direction are very important to obtain the films having large susceptibility, and optical susceptibility depend on the polymerization behavior and the morphology of the films. In the present work, we studied the effect of ion beam irradiation onto the polymerization of diacetylene LB-films.

A moving wall type Langmuir-Blodgett dipping trough was used for dipping multilayer films of diacetylene compounds such as 10,12-heptacosadiynoic acid (HCDA), 10,12-pentacosadiynoic acid (PCDA), 10,12-tricosadiynoic acid (TCDA). The surface pressure for the transfer of monolayer was ca. 20mN/m. The polymerization was carried out with Fe^+ beam at accelerating energy of 60keV and current of 1nA, and electron beam (EB) at accelerating energy of 250keV and current of 20mA, and ultraviolet light (UV).

The X-ray diffraction spectra of poly-HCDA films obtained by Fe^+ irradiation became much sharp and higher order peaks were observed when compared with that of original monomer films. In contrast, The spectra of films polymerized with UV light irradiation became broad and weak, and higher order peaks disappeared with irradiation. Furthermore, the spectra of EB irradiated films were the same as that of original films. Similar phenomena were observed for some other diynoic acids LB-films. The interlayer distance of diacetylene molecules of the films was derived from the value of 2θ at X-ray diffraction peaks. The interlayer distance of diacetylene molecules of the films obtained by Fe^+ beam irradiation was increased significantly when compared with that of original monomer films and those of films irradiated with EB and UV. The increment was 2.8Å for HCDA, 2.2Å for PCDA, 5.4Å for TCDA, respectively. These increments were much larger than those anticipated from the extension of triple bond of original diacetylene to the conjugated double bond and were independent of irradiation dosage.

Similar phenomena was observed when LB-films were treated with Ar^+ beam at accelerating energy of 1keV and current density of $1.6\mu\text{A}/\text{cm}^2$ for a short time although there was no observation of polymerization, and the X-ray diffraction patterns of these films were not varied with EB and UV irradiation. These results show that the conformation of diynoic acid molecules are changed at a very initial period of ion beam irradiation and that the polymerization proceeds in the rearranged state. Such a rearrangement was not obtained in the case of UV irradiation.

INTELLIGENT POROUS MEMBRANES PREPARED BY ION BEAM IRRADIATION

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A porous membrane which shows a reversible change in pore size according to the environmental change was investigated for the first time. Poly(diethyleneglycol-bis-allylcarbonate) known as a sensitive ion and neutron detector was modified by copolymerizing the monomer with pendant α -amino acid group. The polymer made of the latter monomer has a characteristic to change the volume in water according to the environmental temperature change. The copolymer membrane obtained by the combination of 70 % diethyleneglycol-bis-allylcarbonate and 30 % methacryloyl-L-alanine methyl ester was irradiated with Au ion with an energy of 11.4 MeV/u and was etched with 6 N NaOH solution. The membrane provided ion track pores capable of decreasing their cross sectional area reversibly 25 % by changing the water temperature in the range of 0°C and 60°C. This porous membrane is expected as a separator which changes the pore size according to such environmental changes as temperature, pH, and electric field. Further details of the results will be discussed together with the data on vinylcarbonate derivative-containing copolymer membranes.

Stimuli Responsive Membrane Composed of Block Copolypeptide

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An ABA-type block copolypeptide membrane composed of poly(L-glutamic acid) as outer segments (A) and poly(L-leucine) as an inner segment (B) was prepared. According to the observation of electron microscope, the membrane had the phase-separated morphology that the domains consisting of poly(L-glutamic acid) chains are embedded in a continuous matrix of the poly(L-leucine) phase. The reversible conformational change of the poly(L-glutamic acid) from α -helix to random coil induced by changing the pH and KCl concentration of the external medium was presumed to occur in the domains on the basis of the results of infrared absorption spectra and circular dichroism spectra. In the pH dependence of the diffusion coefficients of KCl, NaCl, and LiCl in the membrane, a considerable decrease was found at about pH 4, and thought to result from the conformational transition. In an acidic medium, the permeability of KCl, NaCl, and LiCl was higher than that of glucose, but this order was reversed in higher pHs. These results indicate that the poly(L-glutamic acid) domains in the membrane function as channels for solute transport.

The membrane spontaneously generated electrical pulses under the concentration gradient of KCl in the absence of any external current, voltage, or pressure. The frequency of the electrical pulses was pH depended, and showed a maximum between pH 3 and 4 in the outer KCl solutions. The current-voltage curves of the membrane at the lower KCl concentration were sigmoidal, and hysteresis appeared. This result suggests that the membrane can have two different resistance states which are related to α -helix and random coil of the poly(L-glutamic acid) chain. In the higher resistance state the poly(L-glutamic acid) chains exhibited random coil structure, while in the lower resistance state the chains exhibited α -helix structure. The oscillation mechanism of the membrane potential may be explained by intermittent transport of KCl through the membrane, which is induced by the periodical change of the conformation in the poly(L-glutamic acid) chain.

Electro-sensitive Enzyme Membrane

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An electro-sensitive enzyme membrane has been designed in such a manner as the enzyme activity may be modulated by potential. Fructose dehydrogenase (FDH), which had pyrrolo quinoline qunone (PQQ) at the active site, was selected as model. FDH was electrostatically adsorbed in monolayer on the surface of a platinum electrode. Such a conductive polymer as polypyrrole was deposited in between the adsorbed FDH molecules on the electrode surface by electrochemical polymerization of pyrrole. The polypyrrole/FDH membrane on the electrode surface retained enzyme activity. It is noted that reversible electron transfer is conducted between the electrode and FDH through the conductive polymer which serves as molecular wire or molecular interface.

The enzyme activity of the polypyrrole/FDH membrane was found sensitive to the potential of the electrode. The electro-sensitive enzyme membrane will find feasible applications in intelligent bioreactors and biosensors.

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Molecular design of artificial lectin — Recognition and proliferation of lymphocytes by a novel water soluble polymer having phenylboronic acid moiety

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Lectins are known to bind polysaccharides or glycoproteins specifically and aggregate cells. Since some of lectins can activate lymphocyte subpopulations, these are applied for immunotherapy in clinical medicine. However, lectins have some disadvantages, such as stability, antigenicity in the living system. It is known that boronate anion in the tetrahedral form can easily forms reversible covalent bonds with polyol compounds, such as glucose. The objective of this study is to synthesize a novel water soluble polymer having phenylboronic acid portions as recognition sites of sugar residues existed on the plasma membrane surface of lymphocytes and to characterize its ability as an artificial lectin. Synthesized polymer has fine characteristics such as non-antigenicity, high stability as well as has feasibility of variable molecular design.

Copolymerization of 3-acrylamidophenylboronic acid with acrylamide was carried out in a sealed ampoule under reduced pressure using ammonium peroxodisulfate as initiator in water at 40 °C. The structure of this polymer was confirmed by ¹H-NMR and UV measurement. The copolymer composition was determined by UV measurement of phenyl groups in the copolymer. This polymer was soluble in water and phosphate buffered saline (PBS, pH 7.4).

To estimate the binding ability of poly(AAm-co-PBA) with polyol compounds through covalent bonds of boronate residues with hydroxyl groups, complex formation of poly(AAm-co-PBA) with poly(vinyl alcohol) was evaluated. There observed a considerable increase in viscosity of mixed solution of poly(AAm-co-PBA) (2 wt.-% in PBS) with poly(vinyl alcohol) (2 wt.-% in PBS) at pH 7.4, indicating the complex formation between boronate units with hydroxyl groups in poly(vinyl alcohol). No increase in viscosity was observed when polyAAM homopolymer was used instead of poly(AAm-co-PBA). These results suggest that poly(AAm-co-PBA) can bind with polyol compounds including sugar residues exist on the plasma membrane surface of mammalian cells at pH 7.4.

Mouse lymphocyte aggregation was evaluated by the change in the transmittance of lymphocyte suspension (PBS, pH 7.4) in the presence or absence of poly(AAm-co-PBA). No change in transmittance of lymphocyte suspension was observed by adding polyAAM homopolymer, while obvious increase in transmittance was observed by the addition of poly(AAm-co-PBA) similarly to the addition of typical lectin, Concanavalin A. It is considered that poly(AAm-co-PBA) was bound with lymphocytes through covalent bonds of phenylboronic acid portions with sugar residues exist on the plasma membrane surface, resulting in cellular aggregation

Then, proliferative induction of lymphocytes by the addition of poly(AAm-co-PBA) was investigated. Mouse lymphocytes were cultured with RPMI1640 medium supplemented with 10 % of FCS. Proliferation of lymphocytes was determined by the uptake of ³H-thymidine after 48h cultivation. Dose dependent increase of the ³H-thymidine incorporation was observed in the presence of poly(AAm-co-PBA), while little proliferative response of lymphocytes was observed in the presence of polyAAM homopolymer. It is assumed that the binding of poly(AAm-co-PBA) to glycoproteins on the plasma membrane induced to proliferative response of lymphocytes. From these results, a novel water soluble polymer containing phenylboronic acid portions works as an artificial lectin. This thoroughly synthetic novel polymer is the first example to successfully induce the proliferative response of lymphocytes, and thus, it is suggested that novel polymer with phenylboronic acid residues like poly(AAm-co-PBA) can apply to artificial Biological Response Modifier (BRM).

A Self-Regulated Insulin Delivery System Using Boronic Acid Gel

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Stimuli-responsive hydrogels have been studied as "intelligent materials" which regulate drug release in response to external signals. It is very useful for treatment of insulin dependent diabetes mellitus (IDDM) to achieve controlled insulin release responding to glucose concentration. Boronic acid is known to have an ability to bind with dihydroxyl substances, such as glucose. In this study, the substitution reaction of complexes comprising boronic polymers and hydroxylated insulin with glucose was investigated (Fig.1).

Methacrylamidephenylboronic acid was co-polymerized with acrylamide, and N,N'-methylenebis(acrylamide). Bovine insulin was hydroxylated with tris(hydroxymethyl)aminomethane, and labelled with 9-Anthryldiazomethane. Modified insulin was added to the swelled boronic acid beads. These beads were packed into a liquid chromatography column, and rinsed with the buffer solution. Eluent solutions were alternatively cycled using a computer controlled valve between glucose containing (200 mg/dl) HEPES buffer solution (for 10 min.) and HEPES buffer solution (for 50 min.). The concentration of released modified insulin was pulsatile in response to the repeated pulsatile concentration changes of glucose in the eluent (Fig.2). Another remarkable result is the reproducibility of release pattern of modified insulin, even after multiply repeating cycle. These results are the first to achieve controlled release of insulin induced by a completely synthetic "intelligent" polymer without using traditional glucose-sensitive biopolymers including lectin and glucose oxidase. By further modifications of polymer structure, an on-off chemical system will be achieved which mimick the natural insulin secretion of the β -cell in Langerhans islets.

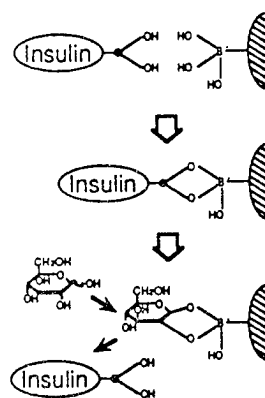


Fig.1 Release Mechanism of Modified Insulin from Boronic Acid Gel

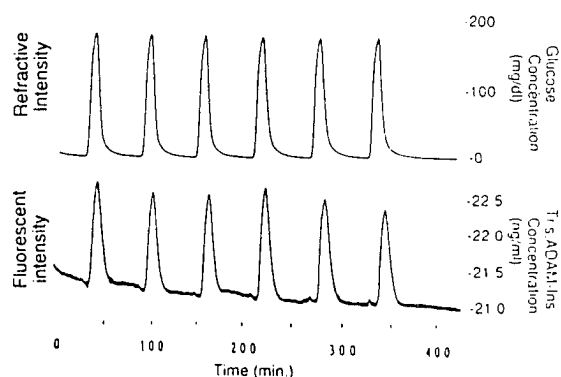


Fig.2 Release of Tris,ADAM-INSULIN from Boronic Acid Gel

**EXOTHERMIC SHAPE MEMORY Ti-Ni PINS
FOR LOCAL HYPERSERMIA SYSTEM
---AN APPROACH TO MULTI-FUNCTIONAL AND INTELLIGENT MATERIAL---**

Yasubumi Furuya*, Yoshikatsu Tanahashi**, Seiichi Orikasa***

ABSTRACT

[I] Exothermic shape memory Ti-Ni pins for local-hypersermia system

From our recent study of the hypersermia method in which the ferromagnetic metal (ferrite) pins are shot into the part of cancer through the pipe-guide outside the patient body, and then the cancerous part can be shrunk by the thermal heat mass induced by the combination of the ferromagnetic pins with the high-frequency electromagnetic induction device. However, if one use the conventional, straight ferrometal pins in this method, the next two main problems arise, that is, (1) The danger of the movement of the shot-pins in the long term. (2) the distribution of temperature within the pin-shot part of cancer becomes non-uniform because of the magnetic anisotropy caused by the correlation between the directions of the straight pins and the magnetic flux. In this study, as one of the countermeasure for these problems, we have developed the advanced local hypersermia system (LHPS) using shape memory Ni-Ti pins coated by ferromagnetic metals. By the thermal self-deformations of pins in the body, it becomes possible for us to get more effective and homogeneous heating in the cancer part without the afraid of the movement of the shot-pins as well as the above-mentioned inhomogeneity of heat-distribution. In the experiment, the shape memory Ni-Ti pins which are attached or enveloped by the very fine ferrite wire in the several ways of close coil, herical and straight type etc. are shot into the gelatin used as a organic model. The rate of the increase in the temperature of the gelatin changes very much depending on the types of ferro-coated Ni-Ti pins. The possibility and characteristics of the new LHPS method are discussed from these results.

[II] An approach to Intelligent Material

Our proposed ferro-coated Ti-Ni shape memory pins is characterized by the following two material functions, that is, (1) Self-exothermal phenomena occurs by the electromagnetically induced eddy current effect. (2) Self-deformation occurs by combination of shape memory effect and the induced heat-generation in ferro-coated Ti-Ni pins. The authors are thinking that our proposed exothermic shape memory Ti-Ni pins can be included in the "Intelligent Material" because it is furnished with the nature of more advanced properties, that is, (1) multi-functionality as well as (2) positive to external stimulus or environments just like a living things and biosphere.

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Langmuir-Blodgett Film by Partially-Spreading Method

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Langmuir-Blodgett Film technique is a stimulus in the research for basic attempts at the development of sensing and information processing with molecular functional elements. It is possible to construct well assembled homogeneous monomolecular layers by the present LB techniques. However, the new technique will be required for a two-dimensional patterning of monolayer to form complex structures as are seen in semiconductor devices.

We will outline our recent studies of the patterning technique of LB films, which we have named "Partially-Spreading Method".

We developed a new bubble-jet pipette specifically for this method. That pipette is able to make a liquid drop of about 3nl. Using the bubble-jet pipette, the Partially-Spreading Method was performed on a contactline that appeared in monolayer deposition. Three phases are in contact at the line: the solid, the liquid and the air. On the contactline, dropped solution containing guest molecules spreads along the contactline.

After evaporation of the solvent, we can obtain a crystallized line of molecules. The host molecules for a buffer layer employed were arachidic acid, arachidic acid methyl ester or stearyltrimethyl ammonium. The guest molecules employed were squarylium. Squarylium was patterned as a line with the line width of $1.5 \sim 15 \mu\text{m}$, and the line volume of $0.06 \sim 4.1 \times 10^{-13} \text{m}^3$. We studied the parameters influencing the line width and volume.

We also carried out the experiment on another type of Partially-Spreading Method. That was performed using the monomolecular layer composed of lipid molecules with permanent dipole moments on a water surface. Local electric fields were applied on the monolayer by placing an electrode on a water surface. These inhomogeneous electric fields produced a distribution of electrostatic energy, giving rise to electrostatic forces parallel to the air-water interface. Lipid molecules on the surface were collected or repelled by attractive or repulsive electrostatic forces.

The host molecules for a buffer layer employed was L- α phosphatidylcholine distearoyl (DSPC). The guest molecules to be implanted was L- α phosphatidylethanolamine distearoyl (DSPE). The dye probe octadecyl rhodamine was to be insoluble in the gel phase, but soluble in the fluid lipid phase. The electrode consists of a tungsten plate with a width of $200 \mu\text{m}$, and length of 10mm. The subphase is grounded via a platinum plate. The domain motions of the guest molecules are observed by a fluorescence microscopy.

The domains of the guest molecules spread using the bubble-jet pipette were gathered locally by the inhomogeneous electric fields. Patterned monolayer was deposited onto a glass plate by the subphase-lowering technique. DSPE was patterned as a line with the line width of $200 \mu\text{m}$. It is necessary to use a sharp-edged electrode to make the line thinner. Moreover, in order to pattern arbitrary shapes, an electrode suitable for doing so is required.

Light Emitting Intelligent Langmuir-Blodgett Films

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Organic dyes show strong absorption bands in UV-visible spectral region. In organic dyes, excited electrons generated by an incident radiation return to the initial ground states without emitting any light. On the other hand, rare earth metal ions display photoluminescence when their electrons are excited, though their quantum efficiencies are rather small. Interestingly, if we could hybridize organic dyes with rare metal ions then the photoluminescent intensity will be significantly enhanced, in which the energy generated by the photoexcitation of a dye will be transferred to the rare metal ion. Furthermore, if we could introduce noncentrosymmetry in the molecular assemblies and fabricate a cavity with a mirror and a grating mirror at both edges of a device, the luminescent light will be amplified in the cavity to permitting laser light. Therefore, a second harmonic light is then generated due to the noncentrosymmetric molecular assembly in the cavity. The second harmonic light can be emitted through the grating mirror. We can classify this newly designed laser emitting device as one of the intelligent materials because it manifests simultaneously three fundamental functions: as a sensor responding to an incident light, a processor allowing the amplification of luminescent intensity, and an actuator for emitting shorter laser light. Therefore, this hybridization of organic dyes with rare metal ions offers multifunctional new devices.

Langmuir-Blodgett technique is one of the most suitable method to hybridize organic dyes with luminous ionic materials. A monolayer can be formed from amphiphilic molecules possessing a light absorption site by including metal ions into the subphase, which can be transferred onto a substrate with highly ordered structure. Luminous ultrathin films capable for dissipating heat can be prepared by using lanthanide metal ions such as Eu^{3+} , Nd^{3+} , etc. In this report, the luminescent characteristics of europium LB films of behenamidobenzoate will be discussed.

Design of the 21st-Century Electron Devices with Intelligent Materials

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In the electronics of the 20th century, an integrated circuit of electron devices with a single function has performed multifunctions with aid of software, while in the 21st century, a device with multifunctionality will perform various functions without relying on integration or software. In other words, the 21st-century electronics should be much simpler than the 20th-century electronics so that it can afford more complex functions with aid of integration or software.

In the 21st century there will be a great demand for materials and devices with high flexibility. With a use of materials whose properties can be modified with external stimuli, careful selection of materials meeting requirements for electron devices will be no longer necessary. Such materials are intelligent materials in a broad sense. A device with intelligent materials can have characteristics modifiable with external stimuli. Such a device is an adaptive device.

This paper gives an overview of the 21st-century electron devices with intelligent materials, and two topics, ferroelectric devices and k-space engineering, are mainly discussed.

The ferroelectric devices in this paper are made of semiconductor and ferroelectric such as PZT and BaMgF₄. For example, when a voltage or current pulse is applied to a gate of a ferroelectric-gate field effect transistor (FET), the ferroelectric gate becomes polarized. The magnitude of the polarization is controlled by the pulse height and width. Once the gate is polarized, charges are induced at the semiconductor surface. Since the channel conductance is affected by the magnitude of the polarization, the device can be used as a programmable resistor element, which can serve to generate modifiable weight synaptic connections for neural network implementations. Even after removal of an electric signal from the gate, the ferroelectric material remains polarized and remembers the state. Since the properties of a ferroelectric material are modified with an electric signal and maintained as long as no signal is applied, a ferroelectric material can be called intelligent, and the device whose characteristic is modified with an electrical signal may be referred to as an adaptive device.

In solid state physics, material properties are well described by the energy-band structure in the k-space (momentum space). Although the present electron devices are operated in the real space, the performance could be optimized if they were controlled in the k-space. The k-space engineering is to design a device whose performance is optimized based on the energy-band structure of materials and effectively utilize materials. For example, in an AlGaAs/GaAs heterojunction bipolar transistor (HBT), electrons are scattered to the satellite valley from the Γ valley at a high electric-field region and lose speed, which limits the performance of a high-speed HBT. However, if the k values of electrons in the transport are controlled by some means, maybe localized electric/magnetic fields and selecting a channel direction, in a direction where scattering to the satellite valleys is unlikely, the performance of an HBT will be optimized. Furthermore, if necessary, the energy-band structure of a material will be manipulated with strain, electric/magnetic field and low dimensionality so that its properties may become suitable for the device. An ultimate goal in the k-space engineering is, however, to synthesize a material whose electronic structure can be modified with external stimuli to meet each demand. Realization of such a material gives birth to an intelligent material in a true sense.

Intelligent Biomaterials in the Future Medicine

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The biological system is composed of several hierarchal levels of integrated molecular system in which purpose-oriented informations are built-in. So, that is one of the excellent model of intelligent materials.

Recently, the health care technology has been so advanced that the paradigm of medical practice might be changed remarkably in the near future. In the future medicine therapeutical methods will be stepped toward (1) Targeting therapy, (2) Bioholonics therapy and (3) Substitution therapy. In each field intelligent biomaterials will contribute to methodological progress of medical treatment in terms of improvement for benefit and decrement of risk and pain for human beings.

In this paper several examples of intelligent biomaterials will be introduced in relation to future medical technology which have been developed in our research group.

(1) Targeting therapy: The efficient anticanceric missile drug of micelle type was developed by conjugating the hydrophobic drug carrier with hydrophilic polyethyleneglycol(PEG) moiety. This polymeric micelle drug can escape from trapping by such a biological surveillance system as macrophages and reticuloendothelial system to reach its destination of cancerous cells effectively.

(2) Bioholonics therapy: The immunological system is playing very important role to keep the homeostasis in bioholonic living body. The specific bio-recognitive material was developed to differentiate B cell from T cell of lymphocyte subgroup. This material is graft copolymer composed of electrically neutral polymer chain and electrically charged polyamine graft exhibiting micro-phase separated structure. By using this copolymer lymphocytes can be separated from each other into subgroups without damage.

(3) Substitute therapy: The stimuli-responsive hydrogels can be applied to artificial secretory gland taking place of diseased organs. The thermo-sensitive hydrogels were developed for antipyretic releasing system and glucose sensitive hydrogels were developed for insulin releasing system.

These intelligent biomaterials contribute to a great extent to make up the ideal curative device, "HOMEOSTAT".

Photochemical Microfabrication and Functionalization toward Integrated Chemical Systems

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Development of lasers and microfabrication techniques has opened a new possibility to create integrated chemical systems, where cascade reactions proceed in a series of spatially-arranged μm reaction sites. As key techniques, microchemical functionalization and fabrication of polymeric materials were explored based on,

- i) Heterogeneous surface photochemical reactions¹⁾
- ii) Laser ablation²⁾
- iii) Scanning electrochemical microscopy (SECM)³⁾
- iv) Chemical vapor deposition (CVD)⁴⁾

and

- v) Laser trapping-spectroscopy-reaction of polymeric microspheres⁵⁾

Micrometer-order fabrication and patterning of polymeric thin films with fluorescent dye molecules were achieved by the above methods of i), ii), and iii). Area-selective CVD was also successful to pattern phthalocyanine derivatives on a copper/silicone substrate for the first time. Three-dimensional manipulation, picosecond spectroscopy, and sub μm fabrication of individual polymeric microspheres dispersed in solution were demonstrated by our currently developed system of laser trapping-spectroscopy-reaction.

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Reaction Processes in Digital Etching

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For fabrication of low dimensional quantum structures, a new etching technique with "self-limiting" characteristics similar to atomic layer epitaxy (ALE) should be developed. We have studied digital etching which has atomic scale controllability, using alternative incidence of etchant gas and low energy ion and electron beams.^{1,2)} To identify the etching mechanism, it is important to clarify the surface processes. In this report, we will discuss the surface processes involved in digital etching of GaAs which contains self-limiting mechanisms, and analyze the experimental results in terms of rate equation analysis.

Digital etching is achieved by repetition of the following processes, adsorption of Cl radicals as an etchant (0.3-0.7sec), excessive Cl purging (10sec), low energy (25eV) Ar ion beam irradiation for surface reaction (1.0-18sec) and purging of etching products (3.0sec).

From experimental results using this sequence, for Cl feeding time greater than 0.3sec, etching does not occur for short Ar ion irradiation time. With increasing Ar ion irradiation time, the etch rate increases, and finally, saturates irrespective of Cl feed time. This saturation property indicates that digital etching involves self-limiting mechanisms.

To explain the experimental results, we assume that Cl physisorption layers are stable and do not easily desorb from the surface. It is also assumed that these physisorbed layers prevent the surface from etching during Ar ion irradiation. These physisorbed Cl layers simply become thinner by Ar ion irradiation, with a beam induced desorption time constant, τ_{dsp}^a , and no etching occurs at the surface until the chemisorbed Cl layer appears. Here, we define X_c as the thickness of the chemisorbed layer. When the adsorbed Cl layers become less than X_c , the etching begins immediately due to the Ar ion irradiation with a reaction time constant, τ_{rac} .

To discuss the surface process in digital etching using rate equation analysis, we consider three kinds of surface conditions, 1) excess Cl physisorbed on the surface which prevents etching ($X \geq X_c + 1$), 2) the adsorbed Cl layer is thin ($X \leq X_c$), and 3) the intermediate condition ($X_c < X < X_c + 1$) in which the above two conditions are mixed should also be considered. Namely, in some areas on the surface the Cl adsorption is X_c and etching is induced by Ar ion irradiation, but in other areas, the Cl adsorption is $X_c + 1$ and etching does not occur. Under this condition, it is assumed that excess Cl rapidly migrates to the bare GaAs surface formed by etching.

From the rate equation analysis, τ_{rac} and τ_{dsp}^a are estimated to be 2.5sec and 1.0sec, respectively. Hence, it can be implied that digital etching includes several etching steps. This differs from conventional reactive ion beam etching (RIBE) in which τ_{rac} is of the order of 100ms. The large τ_{dsp}^a in digital etching implies that a few monolayers of adsorbed Cl are relatively stable even under the low energy Ar ion beam irradiation.

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Photoelectrical responses of dried bacteriorhodopsin in various forms

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Bacteriorhodopsin (BR), which is the sole protein in purple membrane obtained from *Halobacterium halobium*, has the potential to be used as an intelligent biomaterial. Our purpose is to control the photochemical and photoelectrical properties of BRs to use them as an intelligent material. Bacteriorhodopsin acts as a light-driven proton pump; the photo-induced isomerization of the retinal and the subsequent perturbation of the surrounding protein of the retinal lead to transport of a proton. Bacteriorhodopsin takes three forms in acidic solution: the natural purple form (at pH 3 to 7), the blue form (at pH 2 to 3) and the acidic purple form (< pH 2). Bacteriorhodopsin in the blue form can also be obtained by deionization. The various form of BR absorb maximally at 560 nm, 600 nm, and 560 nm, respectively. We examined these three forms BRs in electrodeposited purple membranes by spectroscopy and light-induced electric response measurement of electrodeposited purple membranes.

A water solution in which purple membrane is suspended is sandwiched with two terminals. The purple membrane is then electrophoretically deposited onto an anode such as SnO₂, and dried in a desiccator. This dried natural BR absorbs maximally at 560 nm. Electrodeposited BR of the blue form can be obtained when an excess electrodepositing current is passed through the membrane. The blue BR absorbs maximally at 600 nm. It is believed that membrane deionization by the electrical field make the natural BR blue¹. When a low pH solution (pH 0.4) is added to the dried blue BR, the acidic purple BR form is obtained. The absorption maximum shifts to 560 nm.

The light-induced electrical response of dried BR was measured through the SnO₂ electronode using a mercury drop on the BR as a counter electronode. Operational amplifiers were used as input amplifiers. Excitation flash pulses (with half-life 120 μ s) were produced by a photographic xenon tube with a filter having a cut-off wavelength 540 nm. The photoelectric response of the deposited natural purple BR decays exponentially. The response of the blue BR is bipolar and composed of a spike response signal followed by small amplitude signal with a time course similar to that of the natural BR response. The response of the acidic BR resembles that of the blue BR, although the spectrum of the acidic BR is more like that of the natural BR.

These results indicate that the conformation of BRs is closely related to the photochemical and photoelectrical properties of BRs. We show that BR is a potential intelligent materials which could control the input-output relation through the conformational change of molecules.

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Affinity Latex for the Purification of Specific Proteins

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"Affinity latex" is defined as a polymer colloid in which ligands are immobilized to the particles to separate certain bio-compounds from others through biospecific binding. The sharp response of binding and release of proteins to the ionic strength makes it possible to recover very pure proteins by using the affinity latex. In this study we prepared a sequence-specific DNA-immobilizing latex and applied it for the purification of a transcription factor.

In this system, the following conditions must be satisfied:

1. The bare latex particles must be free from any adsorption of nonspecific proteins.
2. DNA must be immobilized in the manner in which it can catch the desired protein.
3. The resulting hybrid microspheres must be applied in the manner in which it exhibits high binding-selectivity and efficiency without damaging the activity of proteins.

The condition 1 was satisfied with a styrene-glycidyl methacrylate copolymer latex. It was prepared by a soap-free emulsion polymerization followed by post polymerization of additional glycidyl methacrylate. When the glycidyl groups of particles were coupled with ethanol amine, the resulting particle surface suffered no adsorption of proteins.

The conditions for DNA immobilization were searched in terms of DNA chain-length, the ratio of DNA to particle, the reaction pH and temperature, etc. Among them, the chain length of single stranded chain end was found to be the most important factor to govern the amount and mode of DNA immobilization. About 100 DNA chains of 300 base units were immobilized to each particle of 250 nm diameter under the best condition.

A transcription factor E4TF3 was bound to the particles immobilizing sequence-specific DNA at 0.1 M KCl. Occasionally bound nonspecific proteins were washed away with 0.1 and 0.3 M KCl. E4TF3 was released from the particles by washing them with 1 M KCl. It was confirmed that the recovered E4TF3 retained its genetic activity.

Surface Engineering leading to 2-D Biomolecular and Cellular Assemblies

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The precise and functional fixation of biocolloids, such as proteins and cells, on surfaces requires (1) selective fixation of specific biocolloids, (2) positioning of biocolloids at a given portion, (3) density control, (4) orientation of adsorbed or fixed biocolloids and (5) 2-dimensional (2-D) or 3-D assembly. Precise control and combination of these elemental processes can lead to development of molecular or cellular devices. Of elemental processes, (2) and (3) should be totally surface-controllable in nature. In this talk, we summarize our few years' efforts focussing on development of surface process technology, which enables both positioning and density control, and present a few examples of 2-dimensional biomolecular and cellular arrays.

If we can control surfaces one-dimensionally, such surface processing can create gradient and stepwise surfaces, in which density of surface functional group and surface property continuously or discontinuously change, depending on continuous or discontinuous variations of surface processing. This was demonstrated by the liquid/solid interfacial hydrolysis of poly (vinylene carbonate), which was immersed into an alkaline aqueous solution. The resultant film obtained by stepwise-immersion exhibited stepwisely increased hydrophilicity as evidenced by dynamic contact angle measurement. The continuous immersion of the films could provide a gradient surface in which surface hydroxyl group-density and surface wettability gradually change.

Two-dimensional surface control could be achieved by photochemistry. Irradiation of UV-light on O-nitrobenzyl ester of acrylate copolymer resulted in the formation of surface carboxyl group only at irradiated portions. The use of photomasks provided a patterned surface with 2-dimensionally well-define regions. The alternative 2-D surface modification is based on photochemical bonding of phenyl azide group. The copolymer of azide styrene with various vinyl monomers such as dimethyl acrylamide, fluorinated acrylate, sulfonated or aminated styrene altered surface characteristics from highly hydrophobic to hydrophilic, negatively to positively charged, depending on comonomer used.

2-D biomolecular array and cellular array were demonstrated. The former one was achieved by condensation of proteins with surface carboxyl groups generated upon UV-irradiation. The visualized pattern, which was enzymatically stained, was one of examples for 2-D biomolecular array. The 2-D cellular array was formed on a patterned surface with chemical fixation of photoreactive hydrophilic polymer. The cell adhesion, migration and growth was precisely controlled only at non-hydrophilic surface regions.

The precise control of surface processing could provide a basis of a field of biotechnology, in which a surface property plays a dominant role.

Control for cell attachment and detachment by intelligent surfaces

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Recovery of cultured cells from substratum requires the treatment of proteolytic enzymes such as trypsin. The enzymes inflict damage on cell membranes by hydrolyzing various membrane-associated protein molecules, resulting in the impairment of cell function. Therefore, cultured cells sensitive to enzymatic treatment cannot be subcultured. We have developed poly(isopropylacrylamide) (PIPAAm) grafted surfaces as a novel cell culture substrata based on new concept. PIPAAm could be grafted uniformly onto a tissue culture polystyrene dishes (control dishes) by irradiation using an electron beam. PIPAAm has a lower critical solution temperature of about 32°C in water. Over 32°C, PIPAAm grafted surfaces expel water molecules, resulting in reduced polymer volume. Below 32° C, however, it holds water molecules, resulting in swelling. Therefore, the PIPAAm grafted surface reversibly change from hydrophilic to hydrophobic and vice versa by controlling temperature. Cells can adhere on hydrophobic surfaces, but cannot on highly hydrated hydrophilic surfaces. The characteristics of PIPAAm grafted surfaces could be utilized as a substrate to control for attachment and detachment of cultured cells.

Rat hepatocytes, which are highly sensitive to enzymatic treatment, were cultured on PIPAAm grafted and control dishes at 37°C. The ability of PIPAAm grafted dishes to adhere hepatocytes was the same as that of control dishes. Cell growth on both PIPAAm grafted and control dishes were identical. The number of detached cells from PIPAAm grafted and control dishes by low temperature treatment (10°C, 30min) was measured. Nearly 100% of cells were detached and recovered from PIPAAm grafted dishes, while only a few cells were detached from control dish. The temperature dependence of cell detachment was different between hepatocytes and endothelial cells. This indicates that cell-specific separation may be possible by the application of PIPAAm grafted dishes. Hepatocytes recovered by low temperature and trypsin treatment were subcultured on new control dishes. The number of adhered cells after 24 h of cultivation was measured. 80% of the hepatocytes recovered from PIPAAm grafted dishes and 25% of the trypsin-treated cells adhered to new dish. The activities of albumin secretion in primary and subcultured hepatocytes were estimated. Hepatocytes recovered from PIPAAm grafted dishes had remained same activity as primary cells, but activity of cells by trypsin treatment was lower than that of primary cells. We demonstrated that since PIPAAm grafted surface has an inherent hydrophilic-hydrophobic switch induced by temperature change, the attachment and detachment of cultured cells on PIPAAm grafted dishes can be easily controlled thermally. Moreover rat hepatocytes were recovered without the loss of liver-specific functions from PIPAAm grafted dishes and could be successively subcultured.

Artificial Olfactory Sensor on Plural Quartz Crystals

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Recently great interest has been shown in chemical sensors and, in particular, in an "artificial nose" which can categorize fragrances in terms of human reaction to them. One approach to developing such a sensor is to use the human sense of smell as a model. With a view to this, plural piezoelectric sensors coated with organic compounds are attractive because the adsorbate detection and pattern recognition are similar to those in human.

In this work, a set of eight piezoelectric sensors incorporating different polymer materials was fabricated to investigate the adsorption of 37 typical synthetic fragrances in the gas phase. The responses of each sensors to the adsorbate were correlated with human responses to the same fragrance, so-called "psychological effects", in order to design the artificial olfactory sensor.

The eight piezoelectric sensors (humidity dependence $< 5\text{Hz}/\%$) consisted of thin films ($0.8\mu\text{m}$ thick) of (1)polyethylene, (2)poly(2,6-dimethyl-p-phenyleneoxide), (3)polycaprolacton, (4)poly(1,4-butylene adipate), (5)poly(ethylene succinate), (6)phenoxy resin, (7)polycarbonate and (8)polysulfone all coated on quartz crystals (10MHz AT-cut). When the sensors were exposed to a fragrance in vapor form (5-10mg/150ml), the frequency decreased dependent on the weight of adsorbates by 1Hz/ng. The frequency shifts after 6 min normalized by the maximum shift were used as the sensor response data. The human responses to the fragrances were analyzed by grating them on a seven-point scale in terms of descriptive characteristics such as associations with color and emotion.

Adsorbate Response Properties. The sensor responses were investigated using multivariate statistics. Hierarchical cluster analysis employing Euclidean distance was applied to the response data sets to classify the fragrances distinctly. They were classified into three groups, straight-chain, aromatic and unsaturated hydrocarbon, which reflected the chemical structures of the fragrances. This appeared to be related to the solubility of the fragrances in the coating materials. The functional groups in the polymers, such as the phenylene and hydroxy groups, were also found to be related to fragrance classification by principle component analysis. It is very interesting to determine how these responses correlate with the human sense of smell.

Correlation with the Human Sense of Smell. The olfactory sense of the sensor was evaluated with an olfactometer (DAIICHI YAKUHIN), which has been normally used to evaluate the human sense of smell. This sensor response varied for the five test odors and exhibited average recognition and detection threshold concentrations five and four orders of magnitude higher than those for a human, respectively. In spite of their inferior sensitivity, the sensor responses correlated with the human responses. The average ratings in human response tests were analyzed by principle component analysis, and a first component which included such descriptions as pleasant, cheerful and healthy was obtained. Multiple regression analysis using the component scores and the sensor responses as criteria and explanatory variables, respectively, revealed that the sensor responses correlated with the human responses with a multiple correlation coefficient of more than 0.7. These results indicate the possibility of developing an artificial olfactory sensor based on adsorbate detection.

Glucose Sensing Electrode System based on Carbon Paste containing Polyethylene Glycol-modified Enzyme

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Much attention has been paid for the construction of glucose sensing electrode by using carbon paste electrode. Carbon paste electrode (CPE) is of particular interest, because it can be easily prepared and forms a close proximity of the enzymatic site and sensing site. Some hydrophobic enzymes, however, are not expected to exhibit high activity in a hydrophobic carbon paste.

The modification of enzymes with polyethylene glycol (PEG) is useful way for preparing biocatalyst that are active in both aqueous and organic solutions. The PEG-modified enzyme is considered to show an enhanced affinity for the hydrophobic matrix, which would result in higher activity in the matrix than the case of native enzyme. In this paper, we report on the preparation of CPE containing PEG-modified glucose oxidase (PEG-GOD), and that the response to glucose with the CPE.

Two kinds of PEG-GODs were prepared as follows: PEG activated with cyanulic chloride (PEG-CYL) and PEG-succinimidyl succinate (PEG-SS) were separately dissolved in a phosphate buffer (pH 7, 35 °C) and then GOD was added to each solution. After 2 hr, each solution was filtered through ultra-filtration membrane (cut off molecular weight, 30,000), and lyophilized. Enzyme activities of the powders obtained by lyophilization were 15 and 12 U/mg, when PEG-CYL and PEG-SS were used for the preparation, respectively (GOD as received has 100 U/mg of enzyme activity.). GOD content of each PEG-GOD was determined to be 40 % (w/w). These powders were dissolved in the organic media, such as benzene and hexane, as expected.

PEG-GOD was mixed with carbon paste (CP, BAS, Model CP-0) to form CPE: two kinds of CPEs, CPE I and CPE II, were prepared. CPE I was made from PEG-GOD, 1,1'-dimethylferrocene, and CP (1:1:8 by weight), and CPE II was from PEG-GOD and CP (1:10 by weight). For comparison, CPE III was used unmodified-GOD instead of PEG-GOD in CPE I. CPE was 3.2 mm in diameter. Enzyme activities on the surface of CPE I and CPE III were 100 and 20 mU/cm², respectively: the PEG-GOD showed much higher activity than native enzyme does on the surface of carbon paste.

Response with CPE I to glucose was measured: CPE I was immersed in a deoxygenated acetate buffer (20 ml, pH 5), and was applied a potential of +0.4 V vs. Ag/AgCl. Oxidation current was increased after glucose addition, and reached plateau within the 30 s. The current response of CPE I showed linear up to 10 mM glucose. Lower detection limit of CPE I was 0.1 mM glucose (S/N = 5). On the other hand, the linear range obtained on CPE III was 0.5 - 5 mM. These results indicate that the modification of GOD with PEG is effective for widening the dynamic range.

Direct electron transfer between modified GOD and CP was measured in CPE II: CPE II was immersed in a deoxygenated citrate buffer (pH 5.5), and differential pulse voltammetry was performed. Oxidation and reduction current peak was observed at -0.35 V vs. Ag/AgCl. FAD, prosthetic group of GOD, gave oxidation and reduction current peak at -0.41 and -0.36 V, respectively. In contrast, unmodified-GOD showed no current peak in the range between -0.3 and -0.45 V. These results indicate that the direct electron transfer between FAD in GOD and carbon paste matrix proceeds when the enzyme is modified with PEG. CPE II also showed current response to glucose. These PEG-GOD-entrapped CPE can be used for measuring the glucose.

SEALING EFFECT OF A MAGNETIC FLUID AT A CRACK

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ABSTRACT

With the development of space technology and seismology, the problem of the leakage of liquids in various pipelines has stimulated our interest for the safety and excellent performance of several devices. Most liquids leak out through a crack of pipe when the pressure difference between the inside and outside of a tube exists. This paper discusses non-leak liquids as an intelligent material in connection with safety engineering. During the development of the recent high technology, highquality magnetic fluids composed of solid magnetic particles of subdomain size dispersed colloiddally in a liquid carrier have been developed. The magnetic fluids respond well to magnetic fields. This characteristic may be utilized for preventing leakage of a liquid in a pipe.

Experiment was performed to determine the critical gap for liquid leakage. In the experiment, the iron pipe with 19mm inner diameter was divided into two portions. The pipe was filled with magnetic fluid to a selected level was subjected to magnetic fields. A cobalt permanent magnet was used to apply fields in the test. Magnetic fluids used in the experiment were water-based ferricolloid W-35 and its dilution with distilled water. It was found that magnetic fluid in the pipe positioned at the gap by magnetic field(Fig.1). This experimental fact suggests the possibility of non-leakage pipeline system.

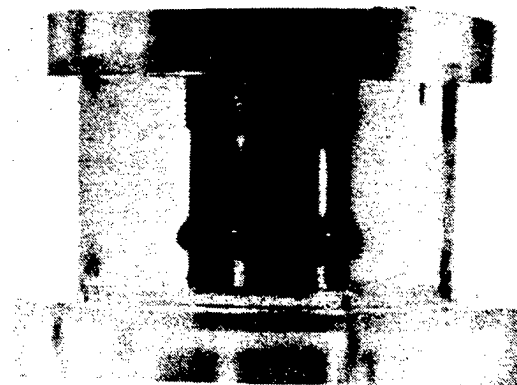


Fig.1 Photograph of the experimental pipe. It can be seen that magnetic fluid bridges the gap. The gap is 1.15mm.

MATERIAL PROPERTIES OF Ti-Ni FIBER REINFORCED/ Al METAL MATRIX COMPOSITE

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ABSTRACT

The equiatomic Ti-Ni alloy has the several superior functional material properties, that is, (1) shape memory effect caused by thermo-elastic phase transformation, (2) super elasticity in the austenite mother phase above the inverse transformation point A_f in higher temperature region, (3) high damping capacity in the martensite phase below M_f point in lower temperature region, (4) high material strength (i.e., high yielding, tensile stress, elongation etc.), (5) high fatigue resistance, (6) high corrosion resistance, (7) high wear resistance etc. From the above mentioned reasons, in this study, we try to use such a very attractive Ti-Ni alloy fibers to produce an advanced fiber-reinforced /Al metal matrix composite (MMC). The experimental results with tensile strength and damping capacity and those dependency on temperature are described. Some theoretical discussions will be done from the view point of thermo-elastic fiber reinforced composite. Finally, we will explain the proposed shape memory Ti-Ni composite concept by relating to the "Intelligent Material".

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Local Strain Sensing Using Piezoelectric Polymer

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Introduction

Needs of the health monitoring system or the self-diagnostic capability for structural components are increasing. In order to realize the system or the capability, highly sensitive and accurate damage sensors should be developed, and also it is desirable that structural materials themselves have the damage sensing function in addition to the durability performance.

The piezoelectric polymer is sensitive to strain leading to the damage and easy to coat the surface of structural materials. Therefore the strain sensing capability of aluminum sheets coated with the piezoelectric polymer was studied, and the preliminary results are presented.

Experimental

Polyvinylidene fluoride (PVDF) films of $9\mu\text{m}$ and $100\mu\text{m}$ thickness which had been stretched and poled in a high electrical field were stuck on the surface of aluminum sheets by epoxy adhesive. Tensile test specimens with small notches were taken from the aluminum sheets and tensile tested.

Changes in electric charge on the specimens during tensile tests were measured using the operational amplifier circuit without decay in the electric charge.

The measuring system including the circuit and a scanning probe is shown in Fig.1. In addition to the quantitative measurements, images of strain distributions formed in the tensile tested specimens were observed using the SEM.

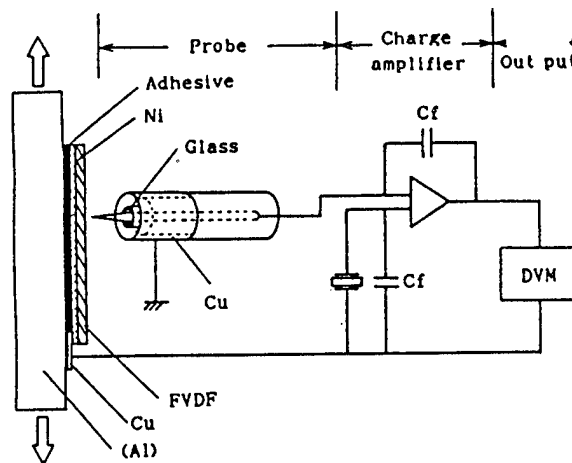


Fig.1. Strain measurement system by the probe method.

Results

The aluminum sheets coated with the PVDF films generate electric charges in proportion to strains, and the electric charges could be measured easily with high accuracy by the probe scanning. Not only plastic strains but also elastic strains around the notches in the tensile tested specimens were determined and strain contour maps were obtained.

The strain distribution is also reflected in the SEM as a voltage contrast image. For the small specimens, strain distributions around the notches were observed clearly in the SEM.

It was proved that the coating of the PVDF film make it easy to detect early stage damage in structural materials.

Optical Properties and Main-Chain Side-Chain Interactions of Quasi-One-Dimensional Organic-Inorganic Mixed complexes

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A halogen-bridged mixed valence metal complex (HMMC) is one of the typical one-dimensional materials which have band gap energies in near-IR, visible, or near UV region. In HMMCs, sequences of metal ions ($M = \text{Pt}, \text{Pd}, \text{Ni}, \text{Pt}_2$ and Ni_2) and Halogen ions ($X = \text{Cl}, \text{Br},$ and I) constitute one-dimensional linear main chains as $X-M-X-M-X-M$. The main chains are surrounded by organic and inorganic side-chain ligand molecules and counter ions. The ground states of HMMCs are commensurate CDW states with periods of twice the metal-metal distances or Mott-Hubbard insulating states. The HMMCs show large third order optical non-linearity and obvious photochromism due to one-dimensional electronic structures. The characteristic feature of HMMCs is that the ligand molecules and counter ions are easily substituted by other molecules and ions.

Since, the band gap energies of HMMCs are not determined by the energy levels of the metal and halogen ions but determined by the competition and cooperation among the physical values such as transfer-energies, electron-electron repulsive energies, and electron-phonon interaction energies, the electronic and optical properties are considered to be much affected by the ligand molecules and counter ions. Therefore, the ligand molecules and counter ions substitution effects have been investigated. It has been found that the substitution of ligand molecules or counter ions causes large changes in the electronic and optical properties of ground and excited states. In bi-nuclear ($M = \text{Pt}_2$) HMMCs, the substitution of ligand molecules causes CDW state - Mott-Hubbard insulating state transition. The substitution of counter ions of these complexes causes large change in band gap energies and photo-absorption line shapes. The formation processes and lifetimes of the mid-gap states which cause the mid-gap absorption bands (photochromism) are also changed by the counter ions substitution. These effects may be explained by the change of main-chain side-chain interaction.

If we can substitute the ligand molecules and counter ions by appropriate external-field reactive molecules, it may be possible to make adaptive intelligent materials using main-chain side-chain interactions.

Thermodynamics of Zirconia System with a Possibility of Intelligent Characters

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The transformation of zirconia has sensitive relations to the physical, chemical, and mechanical properties, especially toughness of itself. By controlling the transformation, it is expected to realize the unique structural material with intelligent characters such as self healing, or self-sensing function on mechanical deterioration. It is important to know the precise information on the energy balance of the system, because it is one of major factors controlling the transformation. However, the available data on the chemical and mechanical energies are very poor. This work is devoted to provide the thermochemical data of zirconia system, and to evaluate the energies on the transformation and mechanical process, and to examine the correlations between the energies and the characters of zirconia system.

A Calvet twin microcalorimeter was used to measure heat of solution of a sample into $3\text{Na}_2\text{O} \cdot 4\text{MoO}_3$ solvent at $970 \pm 2\text{K}$. The samples were dissolved by dropping one rapped by Pt mesh from 300 K, or dipping the sample cell at 970 K. In each solution experiment a 7-15 mg of sample was dissolved in 30 g of melt. The samples used were characterized on chemical compositions, phase relations, specific surface areas, and grain sizes.

From the heats of solution, the enthalpy of t-m transformation of pure ZrO_2 was estimated to be 6.5 kJ/mol at 300K. And the enthalpies of formation of zirconia from m- ZrO_2 and Y_2O_3 were obtained as following; 4.65 (2), 5.0(2.5), 5.75(3), 6.00(4), 4.8(6), and 4.0 kJ/mol(8 mol% Y_2O_3) at 970K. It is shown from this work that (1) the surface energy of t-form is smaller than that of m-form, (2) in ZrO_2 -rich side of ZrO_2 - Y_2O_3 system, t-form is most stable in 3-4 mol% Y_2O_3 of chemical composition, which is corresponding to that realizing the maximum toughness. The strain energies at 970 K were estimated to be order of 0.5 to 1.0 kJ/mol, which were stored in zirconia of 3mol% Y_2O_3 by mechanical grinding treatments for 0.5 to 64 hours. As the internal strain of zirconia may be introduced by both the transformation of t-form and the mechanical treatments, the chemical and mechanical energies are useful as the indication of a toughening ability of zirconia system. The potentiality of zirconia system on intelligent characters will be discussed on these information from a viewpoint of thermodynamics.

Direct Bonding of Zirconia System Without Any Filers

---Basic research for self-healing---

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The transformation of zirconia has sensitive relations to the physical, chemical, and mechanical properties, especially toughness of itself. And the toughness of zirconia was caused by stress-induced phase transformation and by stress-induced microcracking. By controlling the transformation, it is expected to realize the unique structural material with intelligent characteristics such as self-sensing. It is also expected to obtain intelligent characteristics by recovering the microcracks induced by stress. However, it is difficult to characterize each microcrack. And bonding surface can be considered as the model of microcrack. To investigate the possibility of recovering microcracking, it is necessary to characterize the bonding surface. So bonding of zirconia without filers was tried.

For bonding, transparent zirconia, which were supplied by TOSOH Co., Ltd., were used. They were cut into a plate 10mm x 10mm x 1mm and then lapped. The polished surfaces of the samples were contacted each other and then they were fixed by platinum wire.

A pair of samples were put into a platinum capsule (15mm diameter, 7mm long, and 0.5mm thick). The capsule was sealed without evacuation. And it was compressed by HIP both at 1300°C and at 1100°C under 130MPa for 2h.

The sample HIPed at 1300°C was well bonded on the other hand, the sample HIPed at 1100°C was not bonded.

After the bonded specimens were cut perpendicular to the bonding interface, their microstructure was observed by optical microscope and SEM. Mechanical property was measured by Micro-Vickers Hardness.

ELECTRO-DRIVEN CHEMOMECHANICAL BEHAVIORS OF POLYMER GEL BASED ON REVERSIBLE COMPLEX FORMATION WITH SURFACTANT MOLECULES

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Abstract

Electrically-driven chemomechanical polymer gel with high motility is reported. Crosslinked poly(2-acrylamido-2-methylpropanesulfonic acid) (PAMPS) gel was synthesized and chemomechanical behaviors of PAMPS gel in the presence of N-alkylpyridinium chloride (C_nPyCl , $n=4,12,16$) were studied. Under electric field PAMPS gel underwent quick and significant bending and the response was changed drastically by changing alkyl chain length, salt concentration and applied voltage. The mechanism of this behavior is based on a electrokinetic molecular assembly reaction of polymer gel with surfactant molecules caused by both electrostatic and hydrophobic interactions. The results indicate that cooperative complex formation between PAMPS gel and C_nPyCl is responsible for this quick swinging enough to build up chemomechanical actuator. Thus, a gel actuator which "walks" in water with a velocity of 25 cm/min was successfully made.

Gel Composite of Different Functional Polymers

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Various studies have been so far conducted on stimuli-responsive polymers which drastically change their shape and/or characteristics with current, temperature light, chemicals, etc. Poly(vinyl methyl ether) (PVME) is one of the polymers, and is easily crosslinked into gel by irradiation of high energy radiation. PVME gel shows phase transition around 37°C. We already conducted the research on the influence of some chemicals on swelling and shrinking of the gel and PVME porous gel fibers. Two polymer materials, poly(vinyl alcohol) (PVA) superfine fibers and photocross-linkable PVA bearing styrylpyridinium groups, have also been developed to immobilize biocatalysts. These researches are being integrated into a new study on gel composite of different functional polymers.

PVME is mixed with the copolymer of methyl vinyl ether and maleic acid. The mixture is charged into a glass capillary is irradiated and is crosslinked into gel (MVMA). When the gel is immersed in different buffer (pH range 2.51-10.93) at 25°C. At the pH range lower than 6, the MVMA gel swells with pH increase. The maleic acid groups in the gel dissociate more with the increase in pH. That leads to the increase of ion concentration in the gel, that is, the increase of osmotic pressure. The gel does not swell at the pH higher than 6.

As the gel contains ionic groups, the swelling-shrinking behavior of it may be controlled by stimuli other than temperature, such as current, pH, chemicals, etc.

When the mixture of amylo-1,6-glucosidase from *A. niger* and PVME is irradiated by γ -ray, it is crosslinked into gel. The activity of free enzyme increases with the increase in temperature, while the activity of the enzyme entrapped in the gel drastically decreases near the phase transition point of PVME. The immobilized enzyme shows almost no activity over the temperature. As PVME gel is dehydrated and becomes rather hydrophobic at the temperature higher than the transition point, it has a polymer-rich dense structure. That may prevent substrate and product from permeating through the dense membrane. Glucose permeates through the PVM E membrane at the temperature lower than the point but almost no glucose is found to permeate at the higher temperature.

As a preliminary experiment for controlling swelling behavior with the product of enzymic reaction, urease from jack bean is entrapped in PVM E gel. The enzyme also shows the activity dependence on temperature similar to that of the entrapped glucosidase. The enzyme activity at 25°C is around 3 times as high as that at 45°C.

Polymeric micelles as intelligent drug targeting system to cancer

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We have been developing micelle-forming polymeric drugs as a novel type of drug carrier system. An AB type block copolymer composed of hydrophilic and hydrophobic components can form a micellar structure by its amphiphilic character as illustrated in Fig. 1. The hydrophobic drug-binding part forms the hydrophobic core of the micelle, while the hydrophilic part surrounds this core as an outer hydrated shell. Intelligence of this system lies in control of drug delivery by the outer shell of the micelle. Chemical properties of the outer shell and size of the micelle determine delivery of the micelle in living bodies. These factors can be controlled by molecular design of the outer shell which is independent from drug-binding inner core. *In vivo* antitumor activity against murine solid tumor C 26 of adriamycin-conjugated poly(ethylene glycol)-poly(aspartic acid) block copolymer (PEG-P(Asp(ADR))) was revealed to express critical suppression of tumor growth and considerably prolonged life span of the treated mice as shown in Fig. 2. This result indicates that efficient drug delivery to the tumor was done by the novel and intelligent drug carrier system.

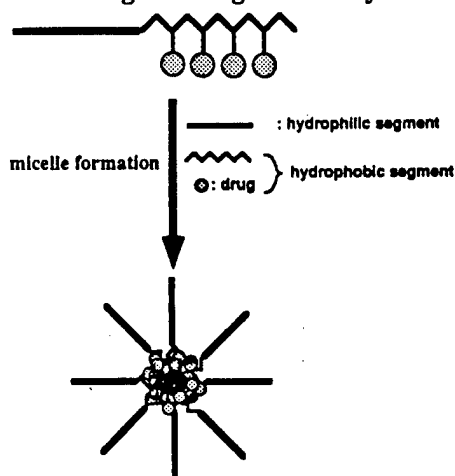


Fig. 1 Concept of micelle-forming polymeric drug

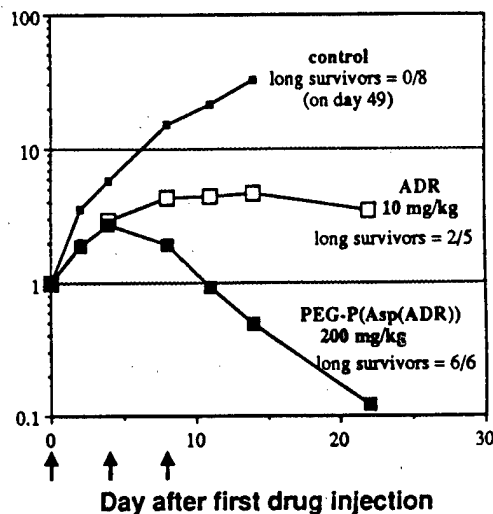


Fig. 2 Anticancer activity against murine C26 tumor

Evaluation of Thermosensitive Polymers As Drug Delivery System

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Drug delivery system (DDS) has been an important subject in pharmaceutical science research. Novel intelligent materials are required in DDS such as controlled release and absorption of drugs, especially products of biotechnology. Polymers are fruitful sources of the materials.

We prepared thermosensitive polymers, poly(N-isopropylacrylamide), which showed specific swelling change in response to temperature in aqueous solvents. The polymers showed swelling on cooling and gel shrinking in an elevated temperature. The volume changes were observed when the temperature was raised until a lower critical solution temperature (LCST) occurred.

Beads of the thermosensitive polymers were prepared and packed in a glass column. The column was thermostated and connected to reversed phase high-performance liquid chromatography (HPLC). The HPLC behaviors of samples were studied in a variety of column temperatures. The samples used as model drugs were antipyretics, albumin and related proteins. The changes of adsorption of the samples to the polymer in aqueous mobile phase with an external temperature were estimated by the behaviors. Membranes of the polymers were prepared. A two chamber diffusion cells were separated with the membrane. The permeations of samples through the membrane were estimated in a variety of temperatures by the concentration of the sample of each cells. The concentrations were determined by HPLC.

The results showed that the thermosensitive polymers are promising materials for DDS such as temperature-controlled drug release.

Site specific polysaccharide-coated liposomes and their applications in medicine

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In order to overcome the disadvantages of liposomes (instability and less site-specificity), liposomes were coated with naturally occurring polysaccharide substituted partly with hydrophobic cholesterol moiety [1]. Polysaccharide-coated liposomes have been found to show an increase in the stability of liposome against external stimuli such as pH, ionic strength, osmotic pressure, and temperature. In addition, the liposome coated with amylopectin or mannan showed a specificity to macrophages in vitro, and significant accumulation in the lungs when intravenously injected.

In the present paper, in order to obtain site-specificity of pullulan (CHP)-coated liposome which did not show any receptor-mediated targetability, we newly synthesized several pullulan derivatives substituted partly with 1-amino-hexose (galactose, mannose, and glucose), hexosamine, or 1-aminobiose (cerobiose and lactose) as cell-recognition site [2]. Egg PC liposomes were coated with these pullulan derivatives. The internalization efficiency of the polysaccharide-coated liposomes by phagocytes (human blood monocytes, neutrophils, rat Kupffer cells), rat hepatocyte, and rat liver cancer cells (AH66) was investigated by RI method. The uptake efficiency of the polysaccharide-coated liposome was correlated with the chemical structure of the terminal sugar residue chemically conjugated to pullulan. Especially, the liposome coated with 1-aminolactose-bound CHP showed relatively high uptake with several tumor cell lines such as liver cancer cell (HuH7 and AH66), lung cancer cell (KNS) and colon cancer cell (FCC) compared with simple CHP-coated or non-coated liposome. In contrary to this, the uptake of the 1-aminolactose-CHP-coated liposome for phagocytes did not increased much compared with that for tumor cells. Furthermore, accumulation of the 1-aminolactose-CHP-coated liposomes intravenously injected into AH66-transplanted mice was also observed. Next, tissue distribution of CHP-coated liposomes for 9L-glioma implanted Fisher-344 rat was investigated [3]. When the liposomes were intracarotidly injected, the distribution of the CHP-coated liposome increased by 4.5 times at tumor and by 2.1 times at ipsilateral brain, and decreased by 4 times at spleen compared with that of non-coated liposome. Furthermore, liposome coated with 1-aminolactose-CHP showed the more accumulation into brain tumor than simple CHP-coated liposome.

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Fatty acid Emulsion stabilized by Hydrophobized Polysaccharide and Its Antitumor Activity

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Several polyunsaturated fatty acids (PUFAs) are known to significantly suppress proliferation of some kinds of cancer cells[1]. In our previous study, strong and selective cytotoxicity of α -linolenic acid (ALA) to human colon cancer cells was revealed[2]. In this work, fatty acid emulsion stabilized by hydrophobized polysaccharide in order to proceed a systemical administration of ALA into body and the antitumor activity in mice were investigated. Sunamoto and his co-workers[3] previously reported that liposome can be effectively stabilized by coating the surface with naturally occurring polysaccharide which bears cholesterol groups in part. Moreover, cholesterol-bearing pullulan (CHP) forms a stable self-aggregate in an aqueous solution, and various hydrophobic substances are incorporated into the hydrophobic domain of the aggregate[4]. Therefore, we employed the CHP-aggregate as a carrier of ALA.

We first investigated the particle size and stability of the newly developed O/W-emulsion. The mixture of CHP and ALA by ultrasonic irradiation at 40 W and 0 °C for 10 min gave nearly monodispersed particles. Since the colloidal stability of CHP/ALA-emulsion, however, was very poor in the presence of serum, we tried to employ trioctanoylglyceride (TriCg) as the stabilizer of CHP/ALA-emulsion. The particle size of the ternary CHP/ALA/TriCg-emulsion depended on the content of ALA and TriCg, and was smaller than that of binary CHP/ALA or CHP/TriCg-emulsion. The stability of CHP/ALA/TriCg-emulsion significantly increased compared with that of others. In the case of CHP/ALA/TriCg (5 : 7 : 3 by wt)-emulsion, no significant change of the turbidity and the particle size of the ternary emulsion was observed even in BSA solution. The antitumor activity of CHP/ALA/TriCg (5 : 7 : 3 by wt)-emulsion was investigated *in vivo*. The emulsion was intravenously administered (dose of ALA, 1.25 or 2.50 mg/mouse) into C3H/He mice which received subcutaneous transplantation of MM46 mammalian tumor cells. Treatment was carried out two cycles with three times injection at 2 days intervals. As a result, a remarkable decrease in the tumor weight was observed without any loss of the body weight. Of course, CHP itself did not show any antitumor activity. The present results indicated that the ternary CHP/ALA/TriCg-emulsion is a very useful system for the treatment of a specific cancer disease.

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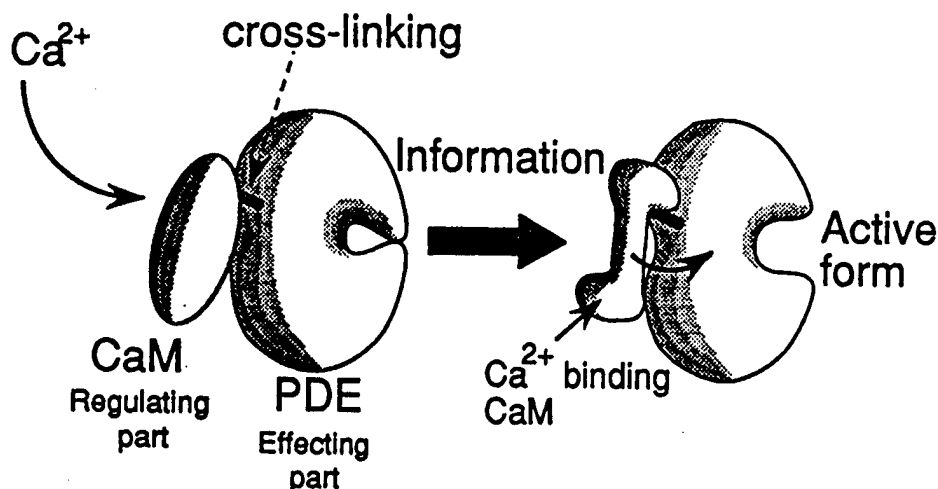
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Stimuli-responsive Protein Assemblies

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Calcium-binding protein, calmodulin, has covalently been conjugated with such a protein as phosphodiesterase with retaining both binding affinity and enzyme activity. The sensing and actuating functions are portioned in the calmodulin and enzyme parts of the protein assembly, respectively. The protein assembly responds to calcium ion in such a manner as the enzyme is activated. It is postulated that calcium ion is bound with calmodulin with a resulting change in its conformation, which is followed by a conformational change of phosphodiesterase. Two different parts of molecular functions have successfully been coordinated in a single protein assembly.



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Intelligent Nonlinear Optical Thin Films Formed by Organic Molecular Beam Deposition

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Nonlinear optical (NLO) thin films are key materials for photonic systems¹⁾ such as optical communications, optical computers and optical neural networks. For example, NLO films with large third-order electrical susceptibility $\chi^{(3)}$ could be used to construct a learning synaptic connection²⁾ due to their optical bistabilities. They will also lead to photonic switching with processing speeds of nearly 1Tb/s because they control the light signal by light. That is, we can disuse the conversion and reconversion of light and electric signals. The realization of such intelligent NLO thin films will therefore leads to drastic improvements in communications systems and information processing systems.

Organic NLO films have great potential for these applications because of their fast response time (100fs). So far, organic polymer superlattices³⁾, polydiacetylene derivatives with oriented structure⁴⁾ and metalophthalocyanines (MPc's) with heat aging treatment⁵⁾ have been reported to have large $\chi^{(3)}$ of $>10^{-10}$ esu. That means that the formation of ordered structure in thin films is necessary to obtain high $\chi^{(3)}$. Molecular beam deposition (MBD) is expected to be a superior thin film formation method because of its high structural controllability as well as its high processability and wide adaptability. We therefore investigated MBD thin film formation of MPc's, which are the most promising candidate.

The MBD chamber was a diffusion-pumped system with a base pressure of less than 5×10^{-10} torr, and the depositions were carried out with a source temperature of 310°C (growth rate of ca. 0.4-0.7nm/min.) and a pressure of less than 1×10^{-9} torr. The substrate was the R(1102) face of sapphire. Film thicknesses of Pc's were ca. 50-120 nm. Three MPc's (M=Cu, VO, TiO) were used after purification by sublimation.

The substrate temperature during deposition strongly effects the crystallinity of the films. Amorphous films of VOPc and TiOPc are obtained at low substrate temperatures of -110°C and 25°C. Phase II crystal films of VOPc and TiOPc, whose ac plane is parallel to the substrate face, are obtained at a substrate temperature of 200°C. On the other hand, CuPc gives a -type crystal films over a wide substrate temperature range from -110°C to 200°C.

Figure 1 shows the influence of substrate temperature on $\chi^{(3)}$ values. The $\chi^{(3)}$ increases with the temperature, and it reaches 1.3×10^{-10} esu for the TiOPc system. The development of ordered structure in the films by increasing substrate temperature is an effective way to enhance the magnitude of $\chi^{(3)}$. These results confirm that the MPc films grown by MBD will be promising candidates for intelligent NLO materials, but further investigation is necessary into the optimum MBD conditions.

We wish to express our sincere appreciation to Professor Hatano, Tohoku Univ., for his kindful provision of TiOPc and thoughtful discussions.

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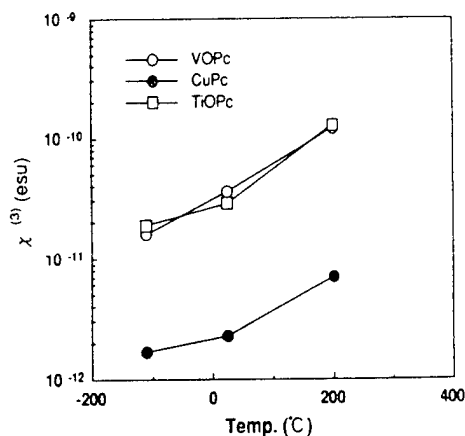


Figure 1. Influence of substrate temperatures on $\chi^{(3)}$ values.

Elemental Molecular Systems for Intelligent Materials

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Molecular systems which Reveal their functions actively and response to multi-stimulations are significant to constitute intelligent materials. Several topics relating to an approach to the intelligent materials are presented.

Multi-mode signal transducer molecules; A new class of chemical signal transducer molecules which have plural transformation modes switchable by independent stimulations.

Photo- and electroactive intramolecular system; A photocontrollable electroactive molecule composed of porphyrin and conducting polymer.

Photoactive molecules cluster; A selfassembled porphyrin cluster which stores electrons and has a long charge separated state.

Designed heterolayers of conducting polymers in 10Å level toward an organic superlattice; Preparative method of ultrathin organic semiconductor heterolayers with desired quantum well and quantum wall, as well as a mesoscopic level.

PHOTOELECTROCHEMICAL INFORMATION STORAGE USING AN AZOBENZENE DERIVATIVE

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Organic molecules having both photochemical and electrochemical reactivities are potentially important in *functional device* research. Azo compound is one of the typical examples, which undergoes two types of reversible processes, photochemical trans-cis isomerization and electrochemical reduction-oxidation. We have investigated the photoelectrochemical behaviors of some amphiphilic azo species in the assembled monolayer films, and found a unique *route-specific hybrid phenomenon* concerning both reactions[1]: the cis isomer is electrochemically reduced to a hydra compound(-NH-NH-) at substantially more anodic potential than the trans isomer, and the hydra compound is exclusively oxidized to the trans isomer. On the basis of such photoelectrochemical hybrid reactions, we have investigated the possibilities for recording optical information[2] and ultra-sensitively counting photons in a photoelectrochemical way.

Our studies on azo compounds have suggested a new avenue for practical applications of organic molecules. For instance, a direct extension of the same studies to the -C=N- and -C=C- systems would be possible because of their similar photochemical and electrochemical behaviors. Molecular designs will play an important role in such studies.

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Information Processing by Intelligent Materials

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Intelligent materials provide a rising and promising subject for study. One of the goals in this area is to develop material systems which can perform information processing in a similar way to silicon LSIs. This paper describes a few ideas for approaches to information-processing material systems.

There are two ways of achieving information processing with materials. One is to use electrical circuits composed of device elements made from the material. The other way is to directly use some physical properties of the material for information processing.

The former way requires construction of integrated circuits using the material instead of silicon, so it will lead to hopeless competition with existing silicon LSIs which are based on a great store of technology and experience. In order to produce new functions, we should choose the latter approach and attempt to employ useful functions in the material itself. I will propose some approaches to direct information processing by materials.

(Holon system) A holonic system⁽¹⁾ is an information-processing system using a synthesizer composed of many unit oscillators (holons), each of which has excitatory/inhibitory interactions with neighbors. It can perform pattern recognition by entrainment among the holons in the synthesizer and the memory. It may be that large holonic systems will be achieved using electron dynamics in 3-dimensional semiconductor superlattices or molecular dynamics in liquid crystals (Fig. 1)

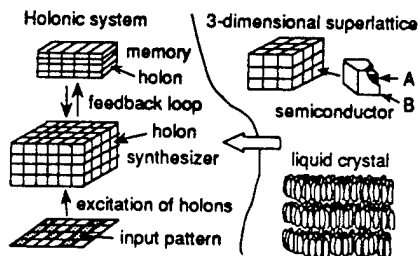


Fig. 1 Material holonic system

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(Neural network) A neural network is an information-processing system characterized by self-organization. It automatically modifies the internal connections (signal channels) by learning to develop required information-processing capability. We can achieve neuro-computing by using conductive high polymers or solid electrolytes provided that we find an effective method of electrically rearranging their network structures (Fig. 2).

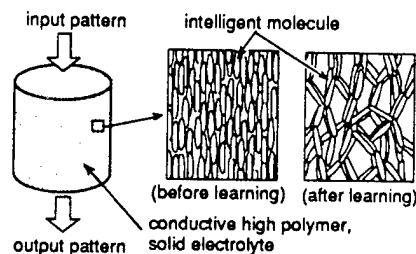


Fig. 2 Material neural network

(Cellular automaton) A cellular automaton⁽²⁾ is an information-processing system consisting of large number of simple identical components (cells) with local interactions. It contains no control center, but is capable of complex behavior. If we can find molecules or crystal units with useful functions for the components, then we can construct large-scale cellular automata by using these materials (Fig. 3). One report has already discussed the possibility of semiconductor-quantum-box cells for the components⁽³⁾.

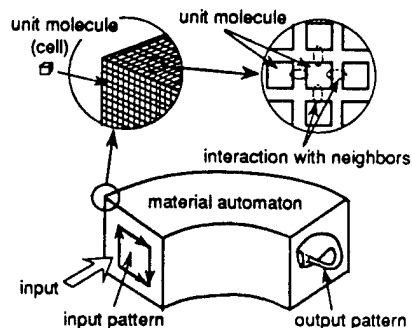


Fig. 3 Material cellular automaton

Ref. (2) "Cellular Automata Machines", MIT Press (1987)

Ref. (3) *Phys.Rev. B*, Vol.37, p8111 (1988)

Artificially Designed Neuron Networks

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The artificially designed neuron network has been investigated with aiming at realizing an interface between electronic devices and the nerve system, and at simulating the information processing in the nerve system.

PC12 cells were selected as model to form neuron networks on the solid surface. In the presence of nerve growth factor (NGF), PC12 cells were differentiated to extended neurites on the surface of an optically transparent In_2O_3 electrode. The outgrowth of the neurites was found to be inhibited, when the electrode potential was controlled above 0.45 V. vs. Ag/AgCl. No appreciable inhibition was observed in the potential range below 0.2 V vs. Ag/AgCl.

The In_2O_3 electrodes were arranged in 20 μm width and 20 μm gap on the glass substrate. The neurites of PC12 cells were linearly aligned along the glass substrate when the electrode potential was controlled at +0.65 V vs. Ag/AgCl. Although the present results are in the first stage of artificially designed neuron networks, a novel method of modulating the outgrowth of neurites has been developed.



Fig. 1

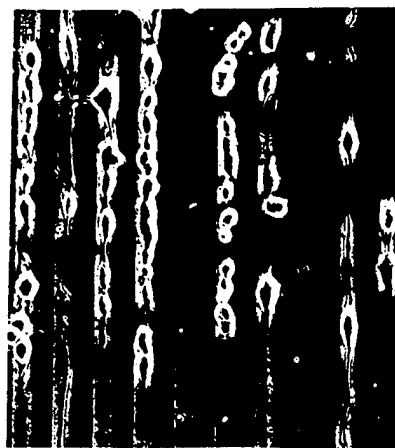


Fig. 2

Fig. 1 Potential-controlled culture at 0.1V vs. Ag/AgCl

Fig. 2 Potential-controlled culture at 0.6V vs. Ag/AgCl

Intelligent Bioelectronic Molecules and Intelligent Biostructures

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The proposed use of biomaterials for electronic device construction (biomolecular electronics) and miniaturization of devices (nanotechnology) represents two separate though related goals in the quest for more powerful information processing systems. These two goals converge in the development of intelligent molecular structures or intelligent molecules. By packaging multiple functionality into a smaller and smaller volume or even a single molecule (integrated functionality), avenues are opened for ultra large scale integration due to the reduced size of the building blocks. The problem of quantum mechanical cross-talk is not crucial, because this very effect is being exploited for technological applications. The development of intelligent materials may make it possible to build a massively distributed parallel processing system.

The present paper examines various aspects of intelligent materials by drawing examples from various natural systems as well as from man-made artificial prototypes. Analysis of the mesoscopic properties of bacteriorhodopsin membranes reveals the inherent cooperative effect that allows the molecule to adapt and function effectively as a proton pump in the presence of a changing environment brought about as a result of the pump's action, i.e., an opposing proton gradient across the membrane. Purple phototrophic bacteria evolved an intelligent microstructure (supramolecular complex) to achieve the same goal of efficient proton pumping. A bioenergetic analysis of these two different proton pumping systems shows that both systems utilize the same principles to minimize back reactions. A comparison between two molecules with similar chemical properties, bacteriorhodopsin and rhodopsin, shows that the molecular functionality (light-induced proton binding) that is used to pump protons in bacteriorhodopsin may be used instead to generate a surface potential in rhodopsin for switching the visual transduction process. In fact, this principle of switching has been implemented in an artificial system with completely different constructs in which ionic conduction through a membrane can be switched by light. The possibility of retooling the same molecular functionality for a completely different task is another facet of molecular intelligence. On the other hand, intelligent molecular design revealed by "reverse engineering" of natural systems can be implemented in the construction of molecular devices utilizing the same principle but completely different materials.

Finally, we propose that there exist multi-facets of molecular intelligence. As beauty exists in the eye of the beholder, material intelligence must be evaluated in the context of intended applications. Nature perfects its designs of various intelligent biomaterials through billions of years of evolution. Since Nature might have optimized the intelligence of a particular molecule on the basis of a completely different set of criteria, it is possible to improve and custom-tailor the material intelligence for the intended purposes through molecular engineering. For example, the molecular functionality of bacteriorhodopsin can be modified by either site-directed mutagenesis or by substitution of synthetic analogs of the chromophore retinal. Such endeavors have led to the development of prototype imaging and holographic devices.

Towards Developing a Human-like Computer

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In recent years, owing to developments in neuroscience, cognitive psychology, information science, information engineering and electronics, great advances have been made in the elucidation of the brain's processing and storage of information. A new field of engineering, "biocomputing", has emerged, which, by exploiting insights from our new understanding of brain function, is endeavouring to produce new information processing systems. Biocomputing is a field of engineering devoted to the development of computers which acquire knowledge through learning and therefore do not require programs. This contrasts sharply with the programming paradigm which characterizes the functioning of present-day computers, and is the same as the functional paradigm of living nervous systems. For this reason, the functions of biocomputers will closely approach those of human beings. Also being pursued for the development of new forms of information processing before the 21st century are systems which have capabilities that are not merely friendly to human users, but that resemble those of human beings. These capabilities are the most difficult ones to implement in computers and include perceptual capabilities similar to man's, the ability to process information rapidly even in complex and ambiguous situations, and the ability of pattern recognition, recursive inference and intuitive thought processes.

In the present talk, I will review questions such as why the development of more human-like computers is essential for human welfare and how they might be developed. Particular emphasis is put on our recent development of a real-time optical system for measurement of nervous activities in the brain at 16,000 sites non-invasively, and its application to rat hippocampus for elucidation of its neuronal circuitry architecture and its activity changes accompanied by inducing long-term potentiation/depression in the circuits.

Micro Flexible Robot Using Reversible TiNi Alloy Thin Film Actuators

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ABSTRACT

It was pointed out[1] that reversible shape memory alloy thin film actuator is very useful for micro sized robot. Reversible TiNi alloy thin film whose thickness is 7 μm was made on a NaCl plate by magnetron sputtering method and its transformation property was tested by DSC method. As the results, the following transformation temperatures are obtained: $A_s=275.6\text{K}(=2.6^\circ\text{C})$, $A_f=294.7\text{K}(21.9^\circ\text{C})$, $A'_s=311.1\text{K}(=38.1^\circ\text{C})$, $A'_f=334\text{K}(=61^\circ\text{C})$ from increasing temperature process, and $M'_s=330\text{K}(=57^\circ\text{C})$ and $M'_f=(27^\circ\text{C})$ from decreasing temperature process. Therefore, this thin film transforms and inversely transforms between R-phase and parent phase according to the temperature between room temperature and about 60°C . This property was also observed as a reciprocal motion by heating and cooling it cyclical. A micron sized flexible arm which has 2 degrees of freedoms was designed on silicon wafer as shown in Fig. 1. In this paper, the properties of reversible TiNi thin film, the IC process of the micro arm and its control will be presented.

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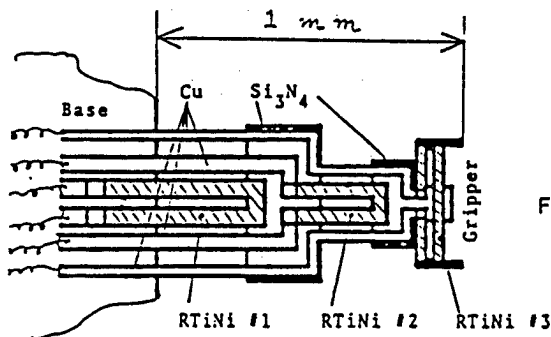


Fig.1 Micro flexible arm using RTiNi thin film on silicon wafer.

STRUCTURE AND CHARACTERISTICS OF AN ULTRA-SMALL BIOMOTOR

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Bacterial cells possess ultra-small motors on their surfaces with which to rotate their flagellar filaments. The motor utilizes the electrochemical energy stored in the proton gradient across the cytoplasmic membrane, and can rotate at more than 15,000 r.p.m. (revolutions per minute). It can rotate in both clockwise and counterclockwise directions and switch the rotational direction in 1 milisec. To analyze the motor function in detail, we have developed a laser dark-field microscopy technique by which high-speed rotation of a single flagellum can be measured. We have also succeeded in controlling the rotation speed by applying an external electric pulse to a bacterial cell that is held at the tip of a micropipette.

The flagellar motor is an organelle consisting of a rotator and a stator that is anchored in the membrane. The rotator is composed of two sets of rings and a shaft which connects to a hook that acts as a universal joint. These components are made of about ten kinds of proteins and many of them have been isolated and biochemically characterized. Several components of the stator have been identified but several proteins have not yet been isolated.

The flagellar motor is the smallest rotary motor in the biological world. The rotator has only 30 nm in its diameter and occupies only about 5×10^4 nm³ in volume. On the other hand, the rotator of the smallest man-made motor which is fabricated on a silicon tip has about 50 μ m in diameter and 5 μ m in thickness, occupying about 10^{13} nm³. The man-made motor is so far 10^8 times larger in volume and 10^6 times in cross section than the flagellar motor.

A flagellar filament is only 24 nm thick so that the rotating filament at high speed can not be observed by ordinary dark-field microscopy. To analyze motor function in more detail, however, measurement of high-speed rotation of a single flagellum with a temporal resolution better than 1 ms is needed. We have developed a new method (laser dark-field microscopy) which fulfills these requirements.

We find that flagella rotate at quite high speed of around 10,000-15,000 r.p.m. Although the average rotation speed of *Salmonella typhimurium* depends on the environmental and physiological conditions, the speed itself is rather stable when the conditions are fixed; its fluctuation is less than 5%.

We have developed a method to hold a single bacterial cell body at the tip of a glass micropipette so that we can transiently change the membrane voltage by applying electric pulses through the micropipette and simultaneously measure the rotation rate of a single flagellum by laser dark-field microscopy. We find that acceleration and deceleration of the membrane containing the motor respectively. The acceleration and the deceleration of the rotation occurred within about 5 ms of the pulse application. This is a direct demonstration that the flagellar motor rotation can be controlled by an external electric field. It also provides a method to measure the voltage-dependent kinetic properties of flagellar motor function, which, in turn, should help us understand the elementary processes of torque generation.

MICROMACHINES

- Concepts, Materials and Mechanisms for New Machines -

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Micromachines are products of microtechnology and nanotechnology, of production on the micro- and submicro-meter scale. Although the production process and applications are still in a primitive stage, micromachines have a wide range of application, from medicine to industrial machines. The creation of micromachines can be thought of either as miniaturizing present technology or of creating new forms on nanolevel.

A microstructure with moving parts should be manufactured in three-dimensional space. The production technologies are inevitably traditional, with top-down method, such as the silicon process and micro electrodischarge machining, while nanomachinery production depends upon autoassembly manufacturing with molecules, representative of protein engineering. Autoassembly technology usually calls for bottom-up technology.

Nowadays, some of the finest industrial products are the large-scale integrated circuit, which includes more than 10^6 electronic parts, and the design size is measured in submicrometers. If we want to produce a fundamental actuator less than $1\mu\text{m}$ in size, we have to create a new technology to build such fine mechanisms. Micromechanisms that can do the work of living organisms and also that of quantum elements is quite appealing and has enormous potential for industrial application. The function of these organisms and elements depends upon the molecular structure and can be analysed quantum physics. Fortunately, recent advances in electrooptical microscope (SXM) technology, representative of scanning probe microscopy, have gradually clarified for us the molecular basis of the bioactuator mechanism. Some SXM devices have been converted to molecular manufacturing tools. From these observation, some bioactuator mechanisms look like the solid state actuator and are possible to designed as crystals. The development of micromachines is certainly requested new novel intelligent materials.

It is sure that the technology will involve many paradigm changes in industrial fields. In the next decade, we may expect many exciting products and fruitful exploration in the micro- and nano-worlds.

Preparation of glucose-responsive polymer complex system having phenylboronic acid moiety and its application to insulin-releasing device

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In recent years, many approaches have been carried out to achieve self-regulated release of drugs by using stimuli-responsive polymers; polymers which change their structure and function reversibly in response to external stimuli related to a particular disease state. In the case of diabetes, a self-regulated insulin releasing system responding to variations in glucose concentration has been strongly desired. To produce such a system, we have developed a novel polymer complex system sensitive to glucose¹⁾. In this system, a phenylboronic acid moiety was incorporated into poly(N-vinyl-2-pyrrolidone) (poly(NVP-co-PBA)) as a sensor molecule for glucose. Interpolymer complexation of poly(NVP-co-PBA) with poly(vinyl alcohol) (PVA) was observed to form a hydrogel due to the covalent linkage of boronate and hydroxyl groups in both constituent polymers. We have further confirmed its dissociation to a sol state responding to glucose. Boronate must firstly be in the tetrahedral anionic form to make covalent complex with diol-compounds. A major limitation of further use of this complex system as an insulin release device under physiological conditions is the relatively high ionization constant ($pK_a=8.86$) of the phenylboronic acid moiety. Only a small fraction of the phenylboronic acid moiety in poly(NVP-co-PBA) was considered to be ionized under physiological conditions ($pH=7.4$), resulting in poor water solubility of this binary copolymer. Thus, an idea to increase the solubility of copolymer in water as well as to form a stable complex with PVA under physiological conditions is required.

In this study, amino groups were introduced into poly(NVP-co-PBA), to increase water solubility as well as facilitate complex formation with PVA under physiological conditions ($pH=7.4$). For this purpose, a ternary copolymer was prepared by the radical copolymerization of NVP with 3-acrylamidophenylboronic acid (AAm-PBA) and N,N-dimethylaminopropylacrylamide (DAPAA) (poly(NVP-co-PBA-co-DAPAA)). The existence of an amino group may contribute to retaining a higher pH condition around the microenvironment of the phenylboronic acid moiety in the gel in comparison with the pH of the bulk solution. This study was designed to demonstrate successful complex formation between PVA and poly(NVP-co-PBA-co-DAPAA) under physiological conditions as well as dissociation in response to glucose. The effect of the addition of glucose to the release of myoglobin from polymer complex gel was also investigated in this study.

Poly(NVP-co-PBA-co-DAPAA) was soluble in water in the range of $pH=3$ to 12, in sharp contrast to poly(NVP-co-PBA) which showed solubility only under alkaline aqueous conditions where the boronic acid group is in a tetrahedral ionized form. The protonated amino group in poly(NVP-co-PBA-co-DAPAA) contributed to increase the solubility of the polymer under physiological and acidic aqueous conditions. Further, poly(NVP-co-PBA-co-DAPAA) formed a stable polymer complex gel with PVA in $pH=7.4$ phosphate buffered solution due to the formation of a covalent linkage between the boronic acid groups in ternary copolymer and diol units in PVA. pH in the gel was measured to be 8.52 by using an ultra-thin electrode, while the bulk solution was buffered to $pH=7.4$. It was clear that the protonated amino groups in the gel contributed to increase the pH of the microenvironment around the boronic acid moiety in the gel to facilitate complex formation with PVA.

The release of myoglobin as model protein from the complex gel was increased immediately after the addition of glucose, due to the transition of gel into sol state, indicating the feasibility of this complex gel as candidate materials for glucose-responsive delivery system for insulin.

Reference 1) S. Kitano, K. Kataoka, Y. Koyama, T. Okano and Y. Sakurai, *Makromol. Chem., Rapid Commun.*, **12**, 227, (1991)

Shrinking Mechanism of Thermo-responsive IPNs Composed of Poly (acrylamide-co-butyl methacrylate) and Poly (acrylic acid) and ON-OFF Drug Release Mechanism

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Temperature responsive ON-OFF drug delivery systems have been investigated using interpenetrating polymer network (IPN)s composed of poly(acrylamide (AAM)-co-butyl methacrylate (BMA)) and poly(acrylic acid) which show positive swelling changes with increasing temperature exhibiting drastic changes at certain temperatures. In this paper, an on-off drug release mechanism from thermo-responsive IPN was studied correlating release behavior to the shrinking mechanism of the IPN.

Ketoprofen was used as a model drug. The drug was loaded into the IPN containing 30 wt% BMA within a PAAm network. Drug release from IPN was performed by fluctuating temperature at fixed times with various temperature intervals. Fig.1 shows the first cycle of release rate change with different temperature intervals. The IPN showed reversible release rate change with temperature fluctuations, as shown in Fig.1. The release rate change with IPN was attributed to diffusivity changes caused by swelling changes in IPN. In some cases, sharp peaks appeared after cooling. Drug release patterns were classified into four types according to the number and time-lag of the peak. Peak appearances seem to be related to the shrinking mechanism of the IPN. At the beginning of the shrinking process, IPN formed a shrunken dense layer (DL) at the surface as the surface was the first part affected by temperature change. At the same time, shrinking yielded an internal pressure (IP) against the DL because of water flux. When DL was strong enough to resist IP, drug release was restricted, resulting in a drastic rate decrease soon after cooling (Type 1). When IP overwhelmed DL strength, water and drug flowed out by a squeezing effect, resulting in a drastic rate increase, followed by a steep rate decrease because of thick dense layer formation (Type 2-4). In the "OFF" release mechanism, the peak appearance in release was determined by DL/IP strength balance.

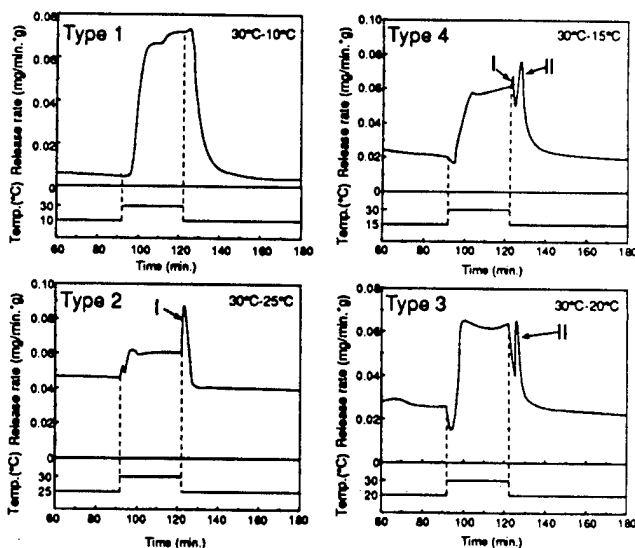


Fig.1 The first cycles of drug release rate changes from IPN-30s in response to temperature changes with different intervals.

"On-off" Switching Mechanism of Pulsatile Drug Release using Thermo-responsive Poly(N-isopropyl acrylamide-co-alkyl methacrylate) Gels.

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Thermo-responsive copolymers of N-isopropyl acrylamide (IPAAm) with alkyl methacrylate (RMA) are capable of "on-off" regulation of drug release in response to external temperature changes. The mechanism of "on-off" switching is clarified in terms of skin formation on the surface of copolymer gels with increasing temperature. To investigate the role of the surface modulated skin and its effect on pulsatile drug release patterns, the surface shrinking process has been regulated by changing the length of the methacrylate alkyl side chain. Release rates of indomethacin from the copolymer gel have been measured continuously by a flow cell system in response to stepwise temperature changes between 20°C (or 10°C) and 30°C. In the switching process of drug release from the "on" state to the "off" state, large temperature changes and thick skin formation of gel lead to large volume changes at the gel surface and resulted in remarkable squeezing of drug from the gel surface (Fig.1). Squeezing was suppressed by small temperature changes and thin skin formation due to long alkyl side chain incorporation (Fig.2). Temperature differences and the length of alkyl side chains were found to be important parameters in controlling the thickness and density of the surface skin layer and the pulsatile drug release pattern.

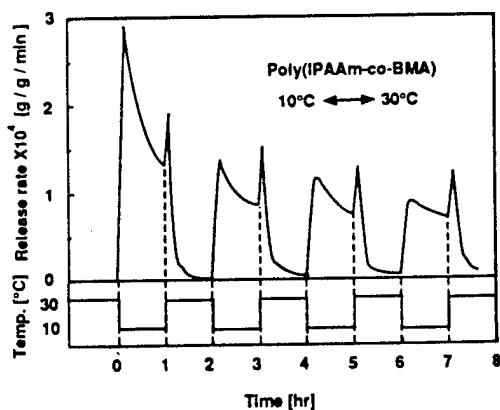


Fig.1 Release rate of indomethacin from poly (IPAAm-co-BMA) in response to stepwise temperature change between 10°C and 30°C in PBS (pH7.4).

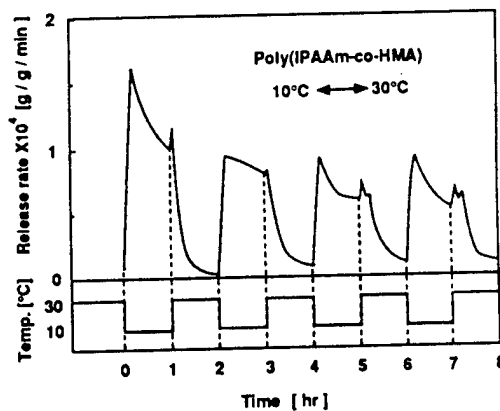


Fig.2 Release rate of indomethacin from poly (IPAAm-co-HMA) (HMA5wt%) in response to stepwise temperature change between 10°C and 30°C in PBS (pH7.4).

DDS Using Polysaccharide Derivatives as Intelligent Hybridizing Materials

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Naturally occurring polysaccharides are an abundant and diverse family of biopolymers and have been widely applied to various fields. The polysaccharides are unique polyhydroxyl compounds that have many chiral sites, and some of them are biodegradable. Since 1982 we have developed and functionalized several naturally occurring polysaccharides and have utilized them in biotechnology and medicine.¹⁻⁸⁾ For example, various hydrophobic polysaccharide derivatives bearing cholesterol moieties were synthesized. The cholesterol-bearing polysaccharide derivatives strongly interact with several molecular assembly systems such as O/W-emulsions, liposomes, lipid monolayers, and black lipid membranes. The polysaccharide-coated liposomes and emulsions are physicochemically stable against external stimuli such as pH, ionic strength, osmotic pressure, temperature and/or polarity of the medium, and in vivo biodegradation by lipases, lipooxidases, and serum proteins. When liposomes as coated with a cell specific polysaccharide were employed, in addition, an excellent receptor-mediated targetability to a specific cell, such as macrophages, monocytes, neutrophils, liver parenchymal cells, and other various tumor cells, was observed. Using these unique and excellent properties of the polysaccharide-coated liposomes the treatment of several infectious diseases in animals, the immunomodulation of alveolar macrophages, and the development of liposomal vaccines have been undertaken. In this paper, a brief overview about the improved DDS using these polysaccharide derivatives recently developed in our laboratory will be made.

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Design of Super Molecular Assembly Recognizable by Hepatic Parenchymal Cells and Its Application to Drug Delivery System (DDS)

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We have synthesized and examined the properties of lactose-carrying polystyrene(PVLA), which has been found as a useful surface coating material for hepatocyte cell culture. PVLA was recognized specifically by asialoglycoprotein receptors on the surface of hepatocyte, that recognize galactose moiety of glycoproteins. Another useful property of PVLA is forming the super molecular assembly in aqueous solution. The PVLA super structure could be potential inclusion carrier of drugs in a target-specific drug delivery system.

In this study, we examined the interaction between hepatic parenchymal cells with PVLA in vitro, ex vivo, and in vivo by using fluorescence probes. In all case, PVLA interacts with hepatocyte specifically. Under ex vivo condition, PVLA was absorbed selectively by parenchymal cells when circulated through an excised liver. Similar results were obtained from in vivo studies.

Moreover, this amphiphilic polymer forms super molecular assembly due to the presence of water soluble lactose residue on hydrophobic polystyrene backbone. PVLA molecular assembly has an inner hydrophobic region that could serve as an ideal binding pocket for the protection of water sensitive drugs. We observed that the formation of super molecular assembly of PVLA and drug models that was bound to hydrophilic or hydrophobic regions of PVLA. These results clearly suggested that PVLA is a potential inclusion carrier of drugs in a target-specific drug delivery system.

Pharmacokinetics and Biodistribution of Polymeric Micelles based on AB block copolymers of Polyethylene oxide and Polyaspartic acid with bound Adriamycin

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The selective delivery of antineoplastics to malignant cells via drug carriers presents one approach to rationale drug therapy (1). To this end, spherical polymeric micelles based on AB block copolymers containing a hydrophobic and hydrophilic segments were prepared. A biodegradable, polymeric micelle system composed of AB block copolymers based on polyethylene oxide (PEG) and polyaspartic acid (P(Asp)) with Adriamycin (ADR) chemically bound via amide bonds was synthesized and characterized. Hydrophobic drugs may be chemically or physically incorporated within the hydrophobic interior of the polymeric micelle. Indeed, loading of ADR of 30 wgt % was obtained without precipitation. The corona region of the polymeric micelle interfaces the biological milieu and for PEG low interaction with biocomponents (e.g., proteins, cells) was expected.

Polymeric micelles have been shown to exhibit high cytotoxic activity *in vitro* and *in vivo* with decreased toxicity (2,3). To establish the mechanisms of the high cytotoxic activity, the pharmacokinetics and biodistribution of radiolabelled PEG-P(Asp(ADR)) micelles was investigated in mice. For this initial study, a one compartment model was used to determine pharmacokinetic parameters for the polymeric micelle and the results compared to free ADR. For PEG-P(Asp(ADR)) with a PEG segment of 4000 molecular weight and P(Asp) with a molecular weight of 1900, respectively, the plasma half-lives for PEG-P(Asp(ADR)) micelles was increased from 1.3 min for free ADR to 70 min. Dramatic differences in the volume of distribution and clearance values were observed for the PEG-P(Asp(ADR)) micelles compared to free ADR. This was consistent with the expected low interaction of the corona region of the polymeric micelle composed of PEG with biocomponents. The effects of composition of PEG-P(Asp(ADR)) micelles on their resultant pharmacokinetics were determined. For PEG-P(Asp(ADR)) micelles less organ accumulation and a greater concentration in the blood compared to free ADR was observed. The selective delivery of ADR by PEG-P(Asp(ADR)) micelles was likely due to decreased uptake into non-target tissue rather than a specific affinity of the polymeric micelles for malignant cells.

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DESIGN OF POLY(α -MALIC ACID)/ADR/SACCHARIDE CONJUGATE EXHIBITING CELL SPECIFIC ANTITUMOR ACTIVITY

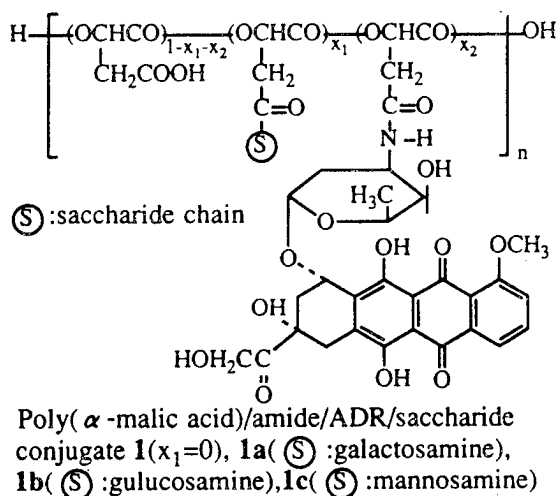
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Since poly(α -malic acid) is interested in the application as a biodegradable and bioadsorbable poly(lactide)types' drug carrier having reactive carboxyl groups, which is able to attach drug and targeting moiety. Adriamycin(ADR) are the most prominent clinical antitumor agents, while its undesirable side-effects have also been cited. We have already reported that poly(α -malic acid) immobilizing 5-fluorouracil(5FU) exhibited excellent survival effect against p388 lymphocytic leukemia cells in mice by intraperitoneal(i.p.) transplantation/i.p. injection.¹⁾ On the other hand, saccharides play an important role in biological recognition. So, in order to achieve the active targeting of polymer/drug conjugates, we have employed sugar residue as targeting moiety and reported the synthesis of poly(α -malic acid)/5FU/saccharide conjugates and cell specific growth-inhibitory effect of poly(α -malic acid)/5FU/galactosamine conjugate against hepatoma cells *in vitro*.²⁾ In this paper, in order to provide the macromolecular prodrug of adriamycin(ADR) reducing the side-effects, having active targetability to tumor cells and exhibiting high antitumor activity, we reports the syntheses of poly(α -malic acid)/amide/ADR conjugate and poly(α -malic acid)/amide/ADR/saccharide conjugates which is expected to have affinity for tumor cells. Moreover, the growth-inhibitory effect of the conjugate obtained against various tumor cells *in vitro* and their survival effect against some tumor cells in mice were investigated.

Three kinds of sugar residue, such as galactosamine, glucosamine, mannosamine, were attached to poly(α -malic acid) *via* amide bonds to give poly(α -malic acid)/saccharide conjugate. The poly(α -malic acid)/amide/ADR conjugate 1 and poly(α -malic acid)/amide/ADR/saccharide conjugate 1a-1c were prepared by reacting the ADR with poly(α -malic acid) and poly(α -malic acid)/saccharide conjugate, respectively.

The cytotoxic activity by poly(α -malic acid)/amide/ADR conjugate 1 and poly(α -malic acid)/amide/ADR/galactosamine conjugate 1a against HLE (human hepatoma) cells and Hela (uterocervical carcinoma) cells were investigated *in vitro*. Moreover the cytotoxic activity of conjugate 1a tend to exhibite higher than that of conjugate 1. The cytotoxic activity of conjugate 1a against Hela cells was not differed from the that of conjugate 1. The effect of short time exposure on the cytotoxic activity of conjugate 1, 1a, 1b, 1c against HLE cells was further examined. Conjugate 1a having galactosamine as a saccharide unit showed high cytotoxicity than the other conjugates. These results suggest that the high cytotoxicity of conjugate 1a was obtained by galactose receptor-mediated selective uptake into HLE cells. Therefore, the poly(α -malic acid)/amide/ADR/galactosamine conjugate can be expected to be used as a macromolecular prodrug having high antitumor activity against hepatoma.

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Highly selective etching for Fluorinated Polyimides by magnetically controlled reactive ion etching (MC-RIE)

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In the micro-machine field, fabrication is usually done by using conventional semiconductor processes. Therefore, the depth of etching during fabrication is shallow, less than 10 μm . The present technique has limitations. Conventional machining techniques are capable of deep fabrication depths, but they are not sufficiently accurate. Consequently, new etching techniques are required for fabrication deeper than 50 μm . To achieve greater fabrication depths, the etching selectivity, that is, the etching rate of etched materials against mask materials, must be one order of magnitude greater than that in conventional techniques.

To achieve this, polyimides, which have excellent resistance against heat and chemicals, have been selected as the material for fabrication. We have studied polyimide film etching rates and etched surface conditions by varying the magnetic field parallel to the cathode surface in magnetically controlled reactive ion etching (MC-RIE). Polyimides can be fabricated to any shape. Further, they can be used to form a resist coating film and the main structural material. Polyimides are etched using an oxygen plasma, and etching rates can be increased by the adding fluorocarbon gas. It is thought that this is due to an increase in the number of oxygen radicals. The formation of hydrogen fluoride is attributed to a reaction between hydrogen in the polyimide and fluorocarbon gas. However, if fluorocarbon gas is added to an oxygen atmosphere, oxidation resistance mask materials, e.g. titanium, silicon, and their oxides corrode more easily. To determine how fluorine activation affects the efficiency and quality of fabrication, the fluorine concentrations of fluorine-bearing polyimide films were varied and then the substrate was etched in oxygen plasma using the MC-RIE system.

For polyimide films with any degree of fluorine concentration, etching rate increases with an increase in the magnitude of the cathode magnetic field. However, at cathode magnetic fields from 0 to 115 Oe, the etching rate does not depend on fluorine concentration but remains constant. The etching rate for a film with 23 wt.% fluorine concentration under a 1600 Oe magnetic field, however, increases over three times when etching is done with no magnetic field. In such cases, the high etching selectivity of above 1000 is obtained using a titanium mask. After etching to a depth of 40 μm on the 23 wt.% fluorine film, the fluorine concentration on the film surface decreases to 5 wt.% as determined by XPS analysis. This indicates that the fluorine in the film reacts with oxygen radicals to increase the etching rates.

SEM observation reveals that the 23 wt.% fluorine polyimide film surface is smooth when high etching rates and high magnetic fields are used. Conversely, the surface of polyimide without fluorine is rough when etching rates are low. With organic plasma etching, reactants such as carbides or polymers, which are hard to vaporize completely from the film surface, often form on the surface. Therefore, the comparative advantages of reactant adhering rate and etching rate depend on the etching conditions. As a result, etched surface conditions are assumed to depend on the effect of masking on the surface residual reactants.

When MC-RIE is used to etch fluorinated polyimide materials, the fabrication efficiency and quality demanded by micro-machine fields are achieved. Thus, the higher rates and increased etching quality might be possible if the fluorine concentration is adequately controlled. This technique can be applied to making lenses with layers having different refractive indexes, and to 3-dimensional structure fabrication by repeating the coating and etching processes, thus taking advantage of the different etching rates of fluorinated polyimides.

Intelligent Materials --- Keys to Technology friendly to Environment and People

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The aim of R & D for intelligent materials is to make technology friendly to environment and people. Intelligent materials are to be developed for saving too much complicated circuits and to minimize the total cost of fabrication, maintenance, and recycling. The functions required for intelligent materials are self-diagnosis, self-adjustment, capability to tuning, etc. Examples of intelligent materials mainly developed by the speaker's group will be introduced. They are p/n contact chemical sensors, carbon fiber IR sensors, and CFGFRP to monitor current and past stress close to fatal breakdown. Recycling design for materials is the first priority to technology leading to the 21st century.

Interfaces in Intelligent Materials

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Intelligent materials (sensors and actuators) are composed of different materials. Extreme conditions (i.e. high temperature, thermal stresses, electrical and mechanical fields) are often applied during processing as well as under service. This may lead to a failure at one of the internal interfaces and, as a consequence, result in the damage of the complete system.

Systematic studies of the structure and chemistry of interfaces relevant for sensors and actuators will be presented. The studies reveal the leading failure mechanisms which can be due to thermally, mechanically, or electrically induced stresses. Chemical reactions at interfaces may occur, depending on the system. The resulting interphase layer influences the performance of intelligent components.

Observations will be reported for different systems, particularly of electro-ceramic actuators and sensors and combinations thereof. Microscopic observations (to the atomic level) used for the explanation of the properties and failure mechanisms of intelligent components will be presented. Emphasis is put on analytical and high-resolution electron microscopy studies. The microstructural results will be used for an explanation of the failure mechanisms and the for degradation of intelligent components.

Preparation of Piezoelectric Paints as Vibration Sensors Coated on the Surface of Structural Materials

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Piezoelectric materials have become increasingly important as sensors and actuators in their applications to the so-called intelligent or smart materials and structures. In such applications, piezoelectric sensors and actuators are embedded within some host materials or bonded to the material surface, thus imparting the vibration sensing and control capabilities to the conventional materials and structures. Usually, piezoelectric materials such as lead zirconate titanate (PZT) ceramics and polyvinylidene fluoride (PVDF) films are used for this purpose.

Piezoelectric paints coated on the surface of structural materials may also be used as a sensor for this purpose, if such paints are successfully prepared. The advantages of such a paint sensor over the PZT and PVDF sensors will be the capability of large area coverage and the applicability to any shape of structural materials. The absence of a bonding layer of adhesives between the sensor and the structural material may be another advantage of the paint sensor from a viewpoint of sensors integrated into materials or structures.

From these points of view, we recently started a study on preparation and evaluation of piezoelectric paints as vibration sensors coated on the surface of structural materials. The preparation of such paints was carried out by using PZT ceramic powder as a pigment and epoxy resin as a binder at the pigment volume concentrations of 25 to 55%. The paints thus obtained were coated on the surface of aluminum beams and cured at room temperature, thus forming thin films having the thicknesses of 15 to 120 μm . Electrodes and lead wires of silver pastes were printed on the surface of these thin films by using a screen mask. A high voltage was then applied to the thin film by using the printed electrode as a surface electrode and the aluminum beam as a ground electrode, thus imparting piezoelectric properties to the thin film.

The piezoelectric activity of the thin film was evaluated from vibration measurement on the film-coated aluminum beam having a strain gage bonded to the beam surface. The vibration measurement was carried out with a dual-channel FFT analyzer by connecting the strain gage to channel A and the thin film to channel B. The measured frequency response function was scaled so as to express the amount of charge generated per unit strain, and was normalized by dividing by the area of the surface electrode, thus giving the piezoelectric activity of the thin film. The highest piezoelectric activity obtained so far is $0.03 \text{ (C/m}^2\text{)/(m/m)}$, which is about 5 times lower than that reported for the PVDF film of Pennwalt Co. Factors affecting the piezoelectric activity will be presented and discussed at the conference.

Development of an Ultra Precision Machine Tool Equipped with a Giant Magnetostriction Actuator

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Recently, single point diamond turning has increasingly attracted special interest for the means to finish the hard and brittle materials such as glass and ceramics. Ultra precision positioning devices with large power and large displacement are required for the diamond turning in order to keep the cracks progressing in the chips and leave no crack on the machined surface. The electrostriction PZT is usually used for the ultra precision positioning device in the measuring instruments such as STM. But, PZT is not suited for the positioning device in the ultra precision machine tools, because it fractures under relatively low pressure. It is well known that the intermetallic compounds with the cubic laves phase structure of the type R_xFe_y ($R=Tb, Dy$) exhibit a giant magnetostriction above 0.1% under the magnetic field. It is a remarkable characteristic in the giant magnetostriction materials that the larger power and larger displacement can be obtained as compared with PZT. In this study, a prototype giant magnetostriction actuator with ultra precision are designed, at the first step. The bias magnetic field and the magnetic moment were computed using FEM. Then the displacement characteristics were examined for the actuator manufactured for trial. The used materials were several alloys of terbium, dysprosium and iron with the composition ($Tb_{0.3}Dy_{0.7}Fe_2$, etc.). It is confirmed through the preliminary test that the giant magnetostriction in actuators makes it be possible to realize the high power stepping drive with ultra fine resolution of nanometer order, which is very hopeful for the micro-movement device. On the other hand, it is an important problem that the control of the thermal deformation due to the Joule heat generated by the variation of the magnetic field. In this study, a temperature controller within 10 m°C was developed for the actuator, at the second step. The ultra precision positioning device was equipped with the temperature controller, and the ultra precision positioning with nanometer errors was realized. Then an ultra precision machine tool was developed for a trial. The equipment is mainly composed of a headstock with a diamond tool which is turned by a main spindle, a saddle with a workpiece, a bed and a positioning system. The saddle is feeded by about 10 nanometer a step with the giant magnetostriction actuator, which is controlled by a personal computer, and the workpiece is cut by a turning diamond tool. It was confirmed that the accuracy of shape and surface roughness was obtained within several nanometers for the cutting depth of micronmeter order. The present machine tool can be also applied to the ultra precision grinding, using a grinder instead of a diamond tool.

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Chemical Sensing System Using Plasma Polymer Films and Pattern Recognition Algorithm

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Abstract

After proposing several plasma polymer films for use in a new intelligent chemical sensor probe, we have studied plasma polymer film formation and intelligent chemical sensing algorithm.

Plasma polymer films have unsaturated bonds and radical sites which cause several unique characteristics. Structural analysis suggests that these films contain high concentrations of π -conjugated structures and stable radicals, which act as interactive sites. These sites, scattered throughout the inert fluorocarbon framework are expected to induce specific interactions with small molecules through π and spin interactions. We have tried to apply our knowledge of these interactions to molecular recognition. For sensing small molecules, these films are deposited on both sides of an AT-cut quartz crystal microbalance (QCM) having a resonant frequency of 9 MHz by radio-frequency (rf) sputtering at 2.0 W/cm^2 of such polymers as polychlorotrifluoroethylene (PCTFE). The QCM is connected to an oscillator circuit and its resonant shift is proportional to the mass of the adsorbed molecules. The affinity of plasma polymer films can be shifted by changing sputtering conditions such as target materials, temperature, or rf power.

For the chemical sensing system, a sensor array having modified films with various sensitivities was used. These films have an affinity not only to one specific kind but to several kinds of molecules. For recognizing of molecules using sensors with overlapping selectivities, a pattern recognition algorithm is needed. First, static and dynamic parameters are extracted from time-dependent sensor outputs, which resemble Langmuir adsorption. Next, these parameters are interpreted and used for classification by employing artificial neural networks. Artificial neural networks can realize arbitrary transformations through learning and be applied as an adaptive signal processing algorithm.

This paper shows that 1) dynamic parameters reflect the interactions between films and target molecules and increase the selectivities and 2) artificial neural networks can learn molecular classification rules and can perform better than principal component analysis. This chemical sensing system, using a pattern recognition algorithm in connection with the plasma polymer films, can make possible new molecular sensing applications such as odor analysis.

CONDUCTIVE ELECTROACTIVE POLYMERS SYNTHETIC, INTELLIGENT MATERIALS

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If one considers that a truly intelligent material must be capable of stimuli recognition, information processing and response generation and that for optimal performance and for ease of manufacture these functions should be integrated into the material during processing, then the number of synthetic intelligent material systems is extremely limited.

To date most forays into the development of intelligent materials have attempted integration of material components with appropriate properties (at a bulk material level). In some limited cases this has resulted in systems and structures with limited intelligence.

However, as reported previously (1-3) we believe that conductive electroactive materials have the ability to perform all of the above functions and that these functions can be integrated at the molecular level during processing.

In retrospect, this suggests that the realisation of the tuneable chemical properties of CEPs and the development of systems which enable function integration when combined produce the first of a new breed of synthetic intelligent material.

In our laboratories we have investigated the electroassembly of these materials in some detail (4). Using the mechanisms elucidated for electropolymerisation means of building up integrated materials have been developed.

Some of these will be discussed in this presentation.

In addition, the recognition (5,6) signal generation and processing (7,8,9) and the response capabilities (10) of conducting electroactive polymers have been the subject of ongoing research in our laboratories. Advances in each of these areas will be reported. These include:

- * **molecular imprinting concepts**
- * **incorporation of biorecognition sites**
- * **electrical signals arising from non-electroactive species**
- * **pattern recognition systems**
- * **triggered release transport mechanisms**

The means by which these functions can be integrated to produce synthetic intelligent materials will be discussed.

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Preparation of stimuli responsive membranes by graft polymerization onto a porous membrane

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A porous poly(vinylidene fluoride) membrane (pore size 0.22 μm) was pretreated by plasma; subsequently, hydrophilic monomers such as acrylic acid and N-isopropylacrylamide were graft-polymerized on the treated surface. Filtration properties of the grafted membranes were examined using a stirred ultrafiltration cell. The grafted polymer chains cover the surface of the membranes. Filtration rates are expected to vary, reflecting the configurations of the grafted chains. The configuration of poly(acrylic acid)(PAA) is very sensitive to environmental pH. Poly(N-isopropylacrylamide) (PIAAm) is soluble in water but has a lower critical solution temperature around 31-33 $^{\circ}\text{C}$. The water filtration rates of the membranes grafted with PAA and PIAAm drastically varied in response to pH and temperature of water respectively. The membrane with the amount of PAA grafting of 133 $\mu\text{g}\cdot\text{cm}^{-2}$ can filtrate out blue dextrane in the pH region of higher than 5 and can not lower than pH 5. These can be changed reversibly from ultrafilter to microfilter and vice versa in response to pH of water. Grafted chains act as a sensor and a valve to regulate filtration characteristics.

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Supramolecular Assembly between functional polysaccharide and proteins

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Creation of new function by an architecture as built with artificial supramolecular assemblies is of considerably interest, especially, in modern materials science. We describe herein a novel example of the formation of supramolecular assembly from two different macromolecular components (polysaccharide derivatives and proteins) by intermolecular non-covalent interaction. We have recently reported that hydrophobized polysaccharides form a sort of self-aggregates in an aqueous medium.¹⁻³⁾ For example, cholesterol-bearing pullulan forms a stable nano-particle (the diameter, 30-50 nm), effectively complexes with various small hydrophobic molecules, and provides a chiral environment.^{2,3)} The CHP self-aggregate was employed as a novel functional host for macromolecules. The complexation between the CHP self-aggregates and various soluble proteins and its property of the macromolecular complexes are presented.

The CHP self-aggregates formed a stable complex with various soluble proteins such as α -chymotrypsin, hemoglobin, peroxidase, myoglobin, and cytochrome c. All the CHP-protein complexes formed were isolable by gel chromatography. The extent of the binding of the proteins to the CHP self-aggregates was affected by molecular weight of the proteins and pH of the medium. Although free α -chymotrypsin was rapidly and spontaneously deactivated because of the self-digestion, the enzyme complexed with CHP self-aggregate, however, nicely maintained the activity and the stability. Self-aggregates of hydrophobized polysaccharides are a new hybridizing material for various macromolecules by self-assembly between two amphiphiles. In addition, it also is possible to further endow cell specificity to CHP by using cell specific polysaccharide derivatives.⁴⁾ Therefore, CHP self aggregates are expected to be utilized as a novel carrier for various biopolymers such as bioactive proteins or enzymes.

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POLYMER GELS INTELLIGENT SOFT MATERIALS AS NEW ENERGY TRANSDUCER

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Polymer gel has attracted considerable attention in recent years. Since it consists of an elastic crosslinked network and a fluid filling the interstitial space of network, it can easily change in size and shape in response to environmental changes such as pH, salt concentration, temperature, and electric field. This is the one of the intrinsic characteristics of polymer gel behaving as a "soft material". Such unique nature can provide a new type of energy transducing system. For example, an ionized gel changes in volume discontinuously when the solvent composition is varied, thus transducing chemical free energy to mechanical work (chemomechanical system).

Quite recently, a series of electroconductive polymer gels swollen in organic solvents were developed and electrochromic and photovoltaic characterizations were discussed. Shape memory and optical-filtration properties using organogels have also been investigated. At present, these are yet embryonic stage but have potentials to be developed as a new type of energy transducing system made of "soft material". A brief survey of recent research activities in this field and future prospect will be described.

Electrically Modulated/Flocculation of Ultrafine Microgels

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Since a theory on polymer gels showed that swelling of a submicron-sized gel could respond within micro-seconds, environmental-sensitive microgels have obtained strong interest from the view point of functional materials for optoelectronic devices. We have devised an electrically controlled pH modulator, which was composed of conductive polymer coated electrodes. The volume of pH-sensitive microgel was electrically controlled in a pH modulator cell. However, in this system the optical effect was too low to apply in practical uses, because of the reduction in the refractive index by the absorbance of water at the swollen state. We present a new strategy to obtain an enhanced optical effect by controlling pH-sensitive microgels.

A concentrated aqueous flocculation of an ultrafine microgel of methyl methacrylate-acrylic acid (MMA-AA) copolymer mixed with poly(L-lysine) (PLL) exhibited rapid and reversible redispersion when the solution was shifted to pH 10-11. In lower pH where PLL was ionized, the microgel underwent bridging flocculation. A pH increase induced PLL to transform from an ionized coil to an helix conformation which resulted in desorption of the bridging PLL to bulk solution from the microgel surfaces. The desorption was assisted by electrostatic repulsion between the microgels, whose charge was converted to be highly negative by the neutralization of the conformational change in concurrence with pH-dependent shrinkage of microgels instantaneously separated an individual microgels, which resulted in remarkably rapid and reversible redispersion. The rate of absorbance change at the transition was as large as 6 abs. unit/sec in the light path of 0.5 cm when solution pH was changed by injecting HCL solution.

A pH modulator, capable of changing solution pH without disturbing stationary state, was employed to ascertain that the rapidity and the reversibility were attainable in a solution of stationary state.

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Mechanical Power Generation by Solvent Sensitive Polymer Gel

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Biological motions are flexible, smooth, smart and dexterous compared to those of man-made machines. The origine of those motions is of course due to the biological motors like muscles or flagella. From this view point to develope a flexible muscle-like actuator could be a breakthrough of advanced robotics, micromachines, medical welfare instruments and so on.

Up to this point gels have never been applied to actuator uses so far because of their slow response, weak force, unfamiliar energy source, poor durability and unestablished peripheral control system. This paper is going to show solvent sensitive chemomechanical material properties and tries to survey critically the problems underlying this research field and the future development.

From the collective diffusion equation the characteristic time constant is proportional to the square of the typical size and to the inverse of collective diffusion coefficient D which is given by the modulus divided by the friction. In order to improve the chemomechanical response one may take several ways realizing 1) thinner films or fibers, 2) high elasticity material, 3) low friction material, 4) porous structure material and so on.

By means of freezing (at -50°C) and thawing (at room temperature) process a mixed aqueous solution of polyvinylalcohol PVA of 1.74M in monomermol, polyacrylic acid PAA of 0.24M and polyallylamine PA1Am of 0.26M turned to a rubber-like elastic gel film in a mold made of two parallel glass plates¹⁾. The elasticity depends on the number of repetition of freezing from 0.02MPa for twice freezing to 0.15MPa for 6 times and 0.56MPa for 100 times in water. In acetone the elasticity increased about 50 times. The process of freezing made a porous gel structure which was controllable by different freezing process. The porous structure improved the chemical mass transfer rate into and out of gel. According to the diffusion equation of mass transfer through gel the diffusion time is roughly proportional to the square of the characteristic size of gel.

In the case of gel film of 10 micrometers thick it shrank in acetone within 0.4sec. The contraction ratio was varied from 30%(no-load) to 10%(0.2MPa) depending on load applied and the gel elasticity. The maximum power density obtained with this film was about 0.1W/g, which is close to the value obtained from skeletal muscle.

Intelligence could be introduced to chemomechanical materials by composing several sequential reactions to realize a continuous cyclic energy conversion or by integrating sensing and effecting functions like to be a logic devices.

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CONTRACTILE POLYMERIC MATERIALS IN THE DESIGN OF A LINEAR ACTUATOR

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ABSTRACT

We have developed a prototype of a polymeric actuator, formed by a parallel bundle of contractile gel fibers. The dynamic response of this actuator to mechanical and chemical stimuli has been studied.

The contractile gel used is polyacrylonitrile (PAN) in form of fibers (Courtaulds Grafil, Ltd, U.K., 13 μm in diameter) cross-linked and ionized to obtain a polyelectrolyte gel structure. The bundle is located inside a rubber container; two electrovalves, controlled by an IBW PC-AT, enable an acid (1M HCl) or basic (1M NaOH) solution to fill the container. Acting on the frequency of stimulation of the electrovalves, it is possible to modulate the actuator's force/elongation output. A measurement protocol has been defined to characterize the dynamic response of this actuator.

A description of the main dynamic characteristics of the actuator has been obtained. The actuator has shown a good weight to power ratio, an attainable degree of miniaturization and built-in compliance. Of particular interest is the analysis of the force versus time response with chemical stimulus; the pH of the bath where the actuator is placed was suddenly changed from 1 to 13 and viceversa. The results show that the maximum force exerted by the actuator is approximately 45 kgp/cm^2 ; from the rest length the actuator takes about 5 seconds to reach the maximum force.

The actuator presents good kinetics and dynamics. Many effort are still required to implement a stable and long life device, which has gentle and precise movements. To satisfy all these needs, thinner contractile fibers made of strong, fatigue resistant gel, new assembly and control technique will be experimented in order to perform applications in many fields such as prosthetics, artificial organs, micromanipulation and robotics.

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